COMPARISON OF EFFICACY OF ORAL VERSUS INTRAMUSCULAR VITAMIN B_{12} SUPPLEMENTATION FOR TREATMENT OF VITAMIN B_{12} DEFICIENCY AND DETERMINATION OF CELLULAR DEFICIENCY OF VITAMIN B_{12} USING SERUM HOMOCYSTEINE AS A SURROGATE MARKER IN PATIENTS WITH LOW NORMAL SERUM VITAMIN B_{12} LEVELS

Dissertation submitted to the
Tamil Nadu Dr. MGR Medical University, Chennai
in partial fulfillment of the requirements for the degree of

DOCTOR OF MEDICINE (D.M)
in
GASTROENTEROLOGY
(Branch IV)

AUGUST 2011

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled **"COMPARISON OF EFFICACY OF ORAL VERSUS INTRAMUSCULAR VITAMIN B_{12} SUPPLEMENTATION FOR TREATMENT OF VITAMIN B_{12} DEFICIENCY AND DETERMINATION OF CELLULAR DEFICIENCY OF VITAMIN B_{12} USING SERUM HOMOCYSTEINE AS A SURROGATE MARKER IN PATIENTS WITH LOW NORMAL SERUM VITAMIN B_{12} LEVELS"** is a bonafide work done by **DR. ARUN R.S.** in partial fulfillment of the requirement of regulations of the Tamil Nadu Dr.MGR Medical university, Chennai for the award of the degree of Doctor of Medicine in Gastroenterology.

Date :

Place: Vellore

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ENDORSEMENT BY
THE HEAD OF THE DEPARTMENT AND THE PRINCIPAL

This is to certify that the dissertation entitled **"COMPARISON OF EFFICACY OF ORAL VERSUS INTRAMUSCULAR VITAMIN B_{12} SUPPLEMENTATION FOR TREATMENT OF VITAMIN B_{12} DEFICIENCY AND DETERMINATION OF CELLULAR DEFICIENCY OF VITAMIN B_{12} USING SERUM HOMOCYSTEINE AS A SURROGATE MARKER IN PATIENTS WITH LOW NORMAL SERUM VITAMIN B_{12} LEVELS"** is a bonafide work done by **DR.ARUN R.S.** under my overall guidance and with the direct guidance and supervision of **DR. ASHOK CHACKO** **M.B.B.S.,M.D.,DM.,MNAMS.,FRCP.**, Professor and Head, Department of Gastrointestinal Sciences, Christian Medical College, Vellore, in partial fulfillment of regulations of the Tamil Nadu Dr.MGR Medical university, Chennai, for the award of degree of Doctor of Medicine in Gastroenterology.

I have immense pleasure in forwarding this dissertation to the Tamil Nadu Dr.MGR Medical university, Chennai .

Dr. Ashok Chacko
Professor and Head
Department of Gastrointestinal Sciences

Date :
Place : Vellore

Dr. George Mathew
Principal
Christian Medical College, Vellore

Date :
Place : Vellore

ACKNOWLEDGEMENT

With deep sense of gratitude, I express my indebtedness to my revered teacher, **Dr. Ashok Chacko**, Professor and Head, Department of Gastrointestinal sciences, Christian Medical College, Vellore, who has been a constant source of inspiration and encouragement and had provided invaluable guidance in the successful completion of this dissertation.

I would like to thank **Dr. Ebby George Simon**, Associate Professor of gastroenterology for his valuable contribution as a co-investigator of the study.

I also express my gratitude to the institutional review board and the **Ethical Committee** of Christian Medical College, Vellore, for granting me permission to conduct this study.

I also thank FLUID for the research grant sanctioned for the study.

I wish to thank **Dr. Amit Kumar Dutta**, for his valuable suggestions regarding statistical analysis of this study.

I am grateful to my mother, my wife, my brother and my colleagues for their everlasting support and constant encouragement.

Last, but not least, I would like to thank my patients without whose consent and cooperation, this would have been an incomplete accomplishment.

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ABSTRACT

TITLE : Comparison of efficacy of oral versus intramuscular vitamin B_{12} supplementation for treatment of vitamin B_{12} deficiency and determination of cellular deficiency of vitamin B_{12} using serum homocysteine as a surrogate marker in patients with low normal serum vitamin B_{12} levels

AIMS AND OBJECTIVES : To compare the efficacy of oral versus intramuscular vitamin B_{12} supplementation for the treatment of vitamin B_{12} deficiency and to determine whether patients with low normal serum vitamin B_{12} levels have vitamin B_{12} deficiency at cellular level, using serum homocysteine as a surrogate marker

MATERIALS AND METHOD : Consecutive patients with vitamin B_{12} deficiency attending department of gastrointestinal sciences and satisfying the inclusion criteria during November 2009 to November 2010 were enrolled in a prospective randomized open label clinical trial to compare the efficacy of oral versus intramuscular treatment and followed up for 3 months. An intention to treat analysis was done using SPSS 16.0 software. Mann-Whitney U test was used for continuous variables and Fisher's exact test for categorical data. For the cross sectional study to determine the cellular deficiency of vitamin B_{12} using serum homocysteine levels as surrogate marker, consecutive patients with a serum vitamin B_{12} <400pg/ml during the above study period were enrolled and Spearman's correlational studies were used.

RESULTS : 60 patients (44male,16 female) were randomized in 1:1 ratio into oral and intramuscular treatment groups. The intention to treat analysis revealed no significant difference in the treatment response between the study groups($p=0.06$). The intramuscular treatment was three times costlier than oral therapy. The most common cause of vitamin B_{12} deficiency was pernicious anaemia. 74% of patients with low normal serum vitamin B_{12} levels had hyperhomocysteinemia suggestive of cellular vitamin B_{12} deficiency.

CONCLUSIONS : Oral vitamin B_{12} supplementation is cheaper than and equally effective as intramuscular treatment for vitamin B_{12} deficiency. The most common etiology for vitamin B_{12} deficiency in a tertiary care hospital setting in India is pernicious anemia. A majority of patients with low normal serum vitamin B_{12} levels (200-400pg/ml) have hyperhomocysteinemia, suggestive of vitamin B_{12} deficiency at cellular level. Serum homocysteine is a useful ancillary test for the diagnosis of intracellular vitamin B_{12} deficiency in patients with low normal serum vitamin B_{12} levels.

KEY WORDS : vitamin B_{12}, homocysteine, randomized trial, intracellular deficiency

INTRODUCTION

There is a high prevalence of vitamin B_{12} deficiency in rural as well as urban population in India (1) . The etiology and risk factors in our population has however, not been adequately studied so far.

The diagnosis of vitamin B_{12} deficiency is hampered by the lack of a gold standard diagnostic test. Studies have shown that serum vitamin B_{12} levels do not accurately reflect its deficiency at a cellular level, especially in the low normal range (2). The cellular deficiency of vitamin B_{12} is associated with elevated homocysteine levels, which is an important risk factor for cardiovascular morbidity (3). Hence it may be important to measure serum homocysteine, which is a cheap and sensitive surrogate marker of cellular vitamin B_{12} deficiency, to identify a subgroup with intracellular vitamin B_{12} deficiency among individuals with low normal serum vitamin B_{12} levels, who may benefit from therapy.

The current recommendation for treatment of vitamin B_{12} deficiency is intramuscular vitamin B_{12} supplementation for an indefinite period, which has serious implications on cost and convenience, in addition to injection related complications. Studies from western countries suggest that high dose oral vitamin B_{12} supplementation may be an equally effective alternative to intramuscular treatment (4). However, the reports favouring oral vitamin B_{12} supplementation should be interpreted with caution in the Indian context, in view of morphological differences in the intestinal mucosa, high prevalence of intestinal parasitic infestations and uniqueness in the composition of intestinal microbiota reported in previous studies(5). So far, there have been no studies substantiating the efficacy of oral vitamin B_{12} supplementation in Indian subjects. Hence there is an imminent need to evaluate the efficacy of cheaper and convenient option of oral therapy compared to the conventional intramuscular treatment for vitamin B_{12} deficiency.

It is also important to identify the treatable etiological factors responsible for vitamin B_{12} deficiency which may enable definitive therapy for a finite period instead of lifelong vitamin B_{12} supplementation. Though pernicious anaemia and food cobalamin malabsorption have been reported to be the common causes in other parts of the world, there could be other potentially treatable causes in the Indian context, on account of the differences in gut characteristics in our population, as discussed above.

The present study was therefore conceived to address these important aspects of vitamin B_{12} deficiency such as comparison of efficacy of oral versus intramuscular treatment for vitamin B_{12} deficiency, elucidation of its causes in a tertiary care setting, and to evaluate whether the patients with low normal serum vitamin B_{12} levels have adequate intracellular function of vitamin B_{12} using serum homocysteine as a surrogate marker.

AIMS AND OBJECTIVES

AIMS AND OBJECTIVES

(i) To compare the efficacy of oral versus intramuscular vitamin B_{12} supplementation for the treatment of vitamin B_{12} deficiency.

(ii) To determine whether patients with low normal serum vitamin B_{12} levels have vitamin B12 deficiency at cellular level, using serum homocysteine as a surrogate marker.

(iii) To identify the causes of vitamin B_{12} deficiency in a tertiary care setting.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

HISTORY

The observation that pernicious anaemia responds to treatment with liver extracts in the early twentieth century heralded the search for the 'anti pernicious anaemia factor', which culminated in the isolation and crystallization of vitamin B_{12} a few decades later. The X-ray structure of vitamin B_{12} was subsequently elucidated in 1955 by Dorothy Hodgkin. It was only in 1972 that the total synthesis of vitamin B_{12} was elucidated after a decade long collective effort of over a hundred scientists (6).

STRUCTURE OF VITAMIN B_{12}

Vitamin B_{12} is a cobalt containing molecule with octahedral structure as shown in figure 1. It is the largest and the most complex of all vitamins.

Figure.1 Structure of vitamin B_{12}

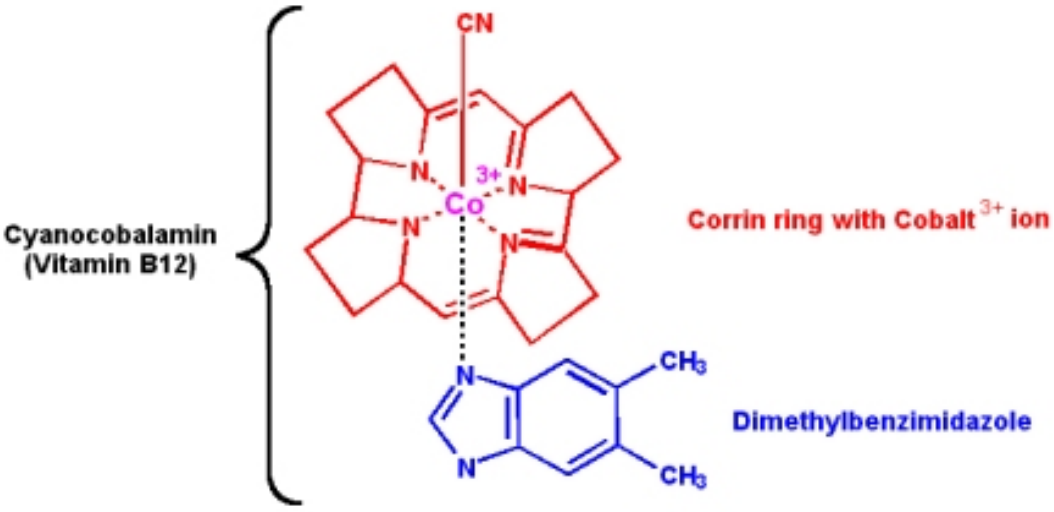


Figure 1

DIETARY SOURCES AND BIOAVAILABILITY

The major dietary sources of vitamin B_{12} are fish, shell fish, meat, milk and eggs. The bioavailability of the vitamin from animal sources is about 50% (except eggs which have a bioavailability of <9%). Though algae and blue green algae contain large amounts of vitamin B_{12}, these compounds are inactive in mammals ('pseudovitamin B_{12}') (7).

The recommended minimum daily requirement for cyanacobalamin is approximately 2.4 micrograms (8).

VITAMIN B_{12} METABOLISM

During gastric digestion, vitamin B_{12} in food is released and forms a stable complex with gastric R-binder or haptocorrin (a glycoprotein of unknown function present in secretions like saliva, gastric juice etc). On entering duodenum, this complex is digested releasing the vitamin which then binds to the intrinsic factor (a glycoprotein produced by parietal cells of stomach). The vitamin-intrinsic factor complex is resistant to proteolysis and travels down to the distal ileum where it binds to specific receptor called cubulin-amnionless in the mucosal brush border. The complex is then taken into the ileal enterocyte where the intrinsic factor is destroyed and the vitamin is transferred to transcobalamin II. The intrinsic factor mediated absorption of vitamin B_{12} in human beings becomes saturated at 1.5 - 2.0 micrograms per meal.

The mechanism of release of the vitamin from intrinsic factor and its exit from the ileal enterocyte is not fully understood (9). About 10-30% of cobalamin in plasma is bound to transcobalamin (referred to as holotranscobalamin, which is the metabolically active form of vitamin B_{12}) and the remaining is transported as a complex with haptocorrin. The

transcobalamin-vitamin B_{12} complex enters the target cells after attaching to the TC II receptor (10)

In addition to the above mechanism, about 1% of orally administered vitamin B_{12} can be absorbed by a passive mechanism throughout the intestine (this is the rationale for oral vitamin B_{12} supplementation)(4)

The vitamin B_{12} taken up by the target cell is usually retained and utilized after conversion into its coenzyme forms –methyl and adenosylcobalamin(11). Within the cell, vitamin B_{12} is crucial for three enzymatic processes

- Methylcobalamin is required as a cofactor for the conversion of homocysteine to methionine. Therefore, vitamin B_{12} deficiency increases serum homocysteine levels.
- Adenosylcobalamin is a cofactor for the conversion of methylmalonyl Co A to succinyl Co A.
- Methylcobalamin is necessary for the conversion of 5-methyltetrahydrofolate to tetrahydrofolate whioch is required for DNA and red blood cell production.

The absorption of dietary vitamin B_{12}, transportation to cells and the physiological role of vitamin B_{12} is outlined in figure 2 (12).

Figure.2 vitamin B_{12} metabolism

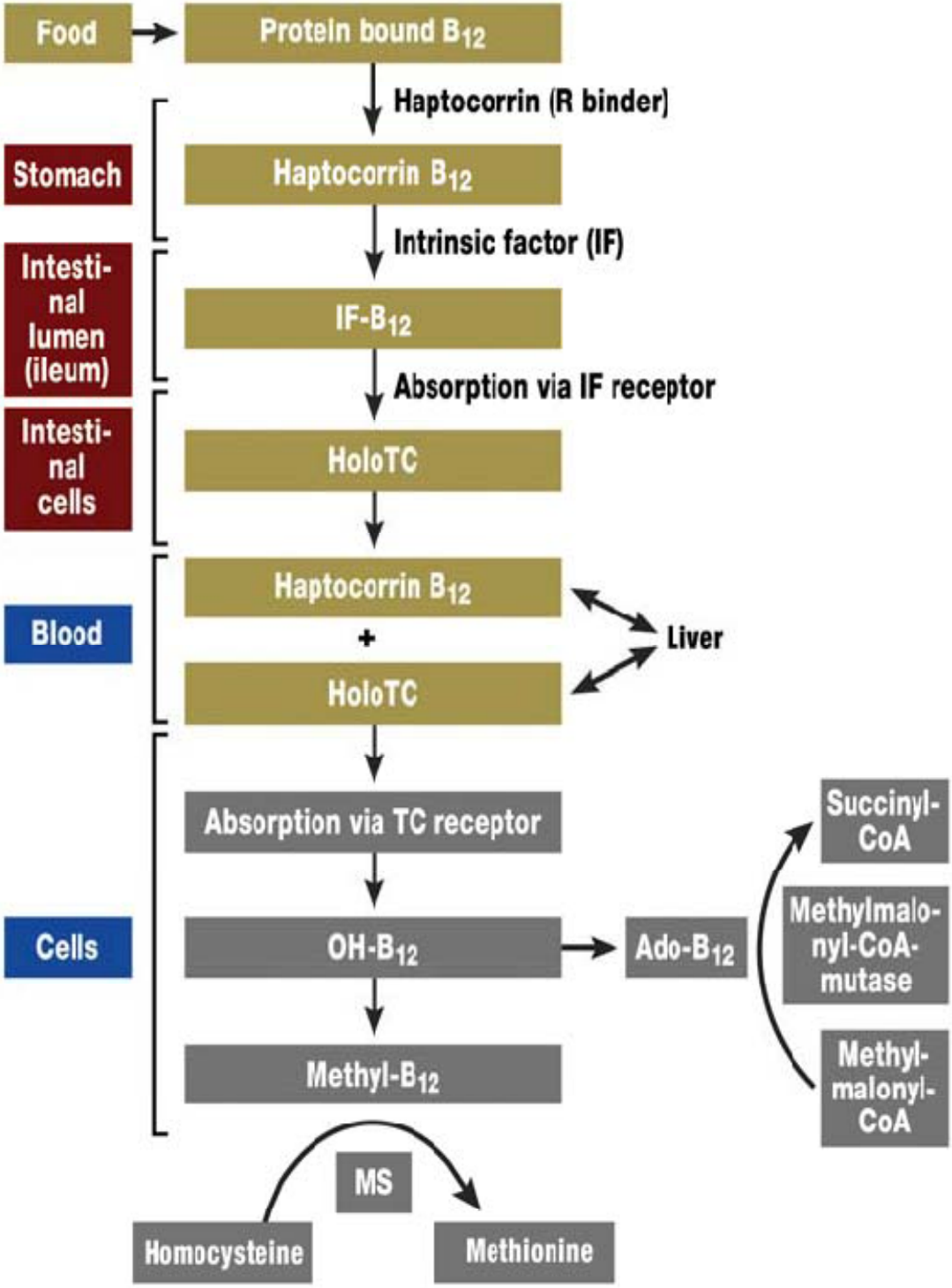


Figure 2

VITAMIN B_{12} DEFICIENCY

Definition

Considerable variation exists in the definition of vitamin B_{12} deficiency owing to the lack of a gold standard test for the diagnosis. However, the widely accepted definitions are listed below (13):

- Serum vitamin B_{12} levels <150 pmol/l (<200 pg/ml) along with clinical and/or hematological features of cobalamin deficiency.
- Serum vitamin B_{12} levels <150 pmol/l on two separate occasions.
- Serum vitamin B_{12} levels <150 pmol/l and serum homocysteine levels >13 mmol/l or methylmalonic acid levels >0.4 mmol/l
  (after excluding renal failure , folic acid and vitamin B_6 deficiencies).
- Serum holotranscobalamin levels <35 pmol/l.

Epidemiology

The estimated prevalence of vitamin B_{12} deficiency varies, depending on the diagnostic criteria used. The prevalence reported from various other countries are listed below (table 1).

Refsum et al, in their study on a selected urban population from Pune, India reported that about 75% had metabolic evidence consistent with vitamin B_{12} deficiency that can only partly be explained by a vegetarian diet(14). In another study on rural as well as urban subjects, Yajnik and colleagues demonstrated that 67% of middle aged men from western India had vitamin B_{12} deficiency(1).

Table 1. Prevalence of vitamin B_{12} deficiency

Author	Year	Number of patients	Cut off serum B12 level (pmol/L)	Prevalence (%)
Blundell et al(15) (UK)	1985	200 geriatric inpatients	<122	10.0
Hanger et al(16) (New Zealand)	1991	204 geriatric subjects in community	<114	7.3
Pennypacker et al(17) (USA)	1992	152 geriatric outpatients	<221 and elevated homocysteine/MMA	14.5
Lindenbaum et al(18) (USA)	1994	548 (Framingham cohort)	<258 and elevated homocysteine/MMA	11.3
Matchar et al(19) (USA)	1994	1599 inpatients and outpatients	<133 and clinical signs, MMA	5.2

Table 1

Natural history of vitamin B_{12} deficiency

Table 2 illustrates the stages in the clinical progression of vitamin B_{12} deficiency(20)

Table 2. Stages of vitamin B_{12} deficiency

Stage 1	**Circulating serum B_{12} levels depleted**	**typically asymptomatic** **can remain so for several years**
Stage 2	**Cellular stores of B_{12} are depleted**	**can remain asymptomatic.** **can also continue for several years.**
Stage 3	**Evidence of biochemical deficiency** **-increases in serum Homocysteine, MMA (methyl malonic acid)**	**Vitamin B_{12} is required for the conversion of these compounds**
Stage 4	**Clinical signs and symptoms apparent**	**manifestations is broad and the sequence varies markedly**

Table 2

ETIOLOGY OF VITAMIN B_{12} DEFICIENCY

Vitamin B_{12} deficiency may result from various inherited or acquired disorders as described below:

I**. Inherited causes of vitamin B_{12} deficiency**(21)

A. Disorders affecting absorption

(i) Congenital pernicious anaemia- characterized by intrinsic factor deficiency. Gastric acid secretion and mucosal architecture are normal. The condition is rare and fewer than 100 cases only have been reported so far. It is treated by lifelong parenteral vitamin B_{12} supplementation.

(ii) Imerslund-Gra¨sbeck syndrome- a rare, potentially fatal condition presenting in children of 3-10years, caused by mutations affecting CUBN gene which encodes cubulin- the high affinity receptor for intrinsic factor-cobalamin complex in ileum- resulting in malabsorption of vitamin B12. More than 250 cases have been reported worldwide so far. Lifelong parenteral vitamin B_{12} supplementation is effective.

B. Disorders of transport

(i) Congenital transcobalamin deficiency- manifests in early infancy with macrocytic anemia, failure to thrive, and/or neurological features. Less than 50 cases have been reported in literature till date. The serum vitamin B12 levels are characteristically normal, as 80% of cobalamin in blood is bound to haptocorrin rather than transcobalamin.

C. Disorders of intracellular metabolism

(i) The conversion of the vitamin to its coenzymes- methyl and adenosyl cobalamin- requires a series of biochemical modifications. Mutations in specific genes have been described for five of the eight complementation groups involved in this process

II. Acquired causes of vitamin B_{12} deficiency

A. Nutritional causes

(i) Malnutrition

(ii) Vegetarian diet- a systematic comparison a group of US, Dutch, and British vegans with nonvegetarians from respective countries found that many of the vegans had significantly lower vitamin B_{12} concentrations compared to the nonvegetarians(22). Subsequently, Dhopeshwarkar and colleagues demonstrated that asymptomatic Indian lactovegetarians, who form the majority of Indian population, had significantly lower serum vitamin B_{12} concentrations than nonvegetarians(23). This was confirmed by later studies from different geographic regions in India(24), as well as the other parts of the world(25).

B. Defects in absorption

(i) Food cobalamin malabsorption- defined as "a syndrome characterized by the inability of the body to release cobalamin from food or intestinal transport proteins, particularly in the presence of hypochlorhydria,where the absorption of 'unbound' cobalamin is normal(26)". It is arguably the most common cause of vitamin B_{12} deficiency in elderly patients(27)

Diagnostic criteria(28):

- Serum cobalamin level < 150 pmol/L
- Result of standard Schilling test (with free cyanocobalamin marked with cobalt-58) is normal, or result of modified Schilling test (using radioactive cobalamin bound to food protein) is abnormal
- No dietary cobalamin deficiency (intake > 2 μg/day)

Associated conditions(13):

- Atrophic gastritis, chronic H pylori infection
- Small intestinal bacterial overgrowth
- Long-term ingestion of H2-receptor antagonists, proton pump inhibitors or biguanides
- Chronic alcoholism
- Gastrectomy, gastric bypass surgery
- Pancreatic exocrine failure
- Advanced age

(ii) Lack of intrinsic factor or parietal cells

- Pernicious anaemia(or Biermer's disease) – a cell mediated autoimmune disease characterised by destruction of gastric fundic mucosa and presence of auto antibodies such as anti parietal cell antibody and anti intrinsic factor antibody(29). It accounts for 15-50% of cases of vitamin B_{12} deficiency. Associated conditions include autoimmune disorders like vitiligo, dysthyroidism, Addison's disease, Sjögren's syndrome as well as gastric neoplasms like adenocarcinomas, lymphomas and carcinoid tumours(30).
- Atrophic gastritis
- Gastrectomy

(iii) Ileal disease

- Crohns disease
- Ileal resection

(iv) Biologic competition

- Bacterial overgrowth
- Fish tapeworm infestation

C. Defects in transport

(i) Transcobalamin II deficiency

CLINICAL FEATURES (31)

The majority of patients with vitamin B_{12} deficiency are asymptomatic. Less than 10% of patients have one or more of the classically described manifestations, which are listed below.

- **Hematologic**
    - Megaloblastic anemia
    - Pancytopenia (leukopenia, thrombocytopenia)
- **Neurologic**
    - Paraesthesias
    - Peripheral neuropathy
    - demyelinating disease of dorsal columns and corticospinal tract
- **Psychiatric**
    - Irritability, personality change
    - Mild memory impairment, dementia
    - Depression
    - Psychosis
- **Cardiovascular**
    - increased risk of myocardial ischaemia and cerebrovascular accidents

Increasingly, the existence of "iceberg phenomenon" for vitamin B_{12} deficiency has been recognized and the entity of subclincal vitamin B_{12} deficiency has been defined as " an asymptomatic state of vitamin B_{12} deficiency where metabolic deficiency is demonstrable" (32). Table 3 illustrates the features of subclinical cobalamin deficiency.

Table 3. Comparison of clinical and subclinical vitamin B_{12} deficiency

	Clinical deficiency	Subclinical deficiency
Symptoms and signs	Present	Absent (may have electrophysiological changes)
Serum B12 levels	Low in 97% (<200pg/ml)	Usually lowl, but may be low normal
Frequency	<10% with serum B12 less than 200pg/ml	70% with serum B12 <200pg/ml 30% serum B12 200-400 range
Course	Progressive	Unknown, may progress slowly
Cause	Identifiable in most cases	Identifiable only in about 50%
Treatment	Mandatory	Advisable, dose unclear

Table 3

DIAGNOSIS

There is no universally accepted gold standard diagnostic test for vitamin B_{12} deficiency. Therefore, the diagnosis is based on a constellation of clinical, haematological and biochemical parameters. Various serum biomarkers of vitamin B_{12} deficiency have been reported to be useful in this regard.

Serum Biomarkers of vitamin B_{12} deficiency(33)

Though serum vitamin B_{12} estimation is widely used cost effectively as the diagnostic test of choice, it has only a limited sensitivity and specificity, especially in persons with vitamin B_{12} levels less than 400 pmol/L(low normal/ borderline range)(25).

In a study by Solomon et al, the median intraindividual variation in measured serum vitamin B_{12} levels was 23 % and absolute differences >100 pmol/L on repeat testing was noted in 21 % patients (34). Stabler et al estimated that 5-10% of patients with serum vitamin B_{12} levels between 200 and 300 pg/mL and 0.1% to 1% with levels higher than 330pg/mL have a tissue deficiency of cobalamin(2).

The serum levels of homocysteine and methyl malonic acid are elevated in vitamin B_{12} deficiency and have been shown to be reliable markers for tissue deficiency of cobalamin(35)

The various serum markers useful for the diagnosis of vitamin B_{12} deficiency are listed below in table 4.

Table.4 Serum biomarkers of vitamin B_{12} deficiency

Marker	Remarks
Serum homocysteine	High sensitivity, cheap, easily available
Serum methyl malonic acid	High sensitivity as well as specificity Requires mass spectrophotometry Available only at select centres
Plasma holotranscobalamin	Earliest marker to be elevated

Table 4

Usefulness of serum homocysteine in the diagnosis of vitamin B_{12} deficiency

Serum homocysteine estimation is a cheap, widely available and sensitive test (95.9%) for the detection of cellular deficiency of vitamin B_{12} and correlate well with methyl malonic acid levels (36). Studies have demonstrated a strong inverse correlation between serum levels of vitamin B_{12} and homocysteine(14),(37).

However, elevation of serum homocysteine may also occur in smokers, alcohol abuse, renal failure and folate deficiency and these should be excluded before attributing it to vitamin B_{12} deficiency. Serum homocysteine has been reported as a useful adjunct for the determination of cellular vitamin B_{12} deficiency in patients with low normal/ borderline serum vitamin B_{12} levels(33).

Functional tests of vitamin B_{12} absorption(33)

(i) Schilling's test : considered as gold standard functional test of cobalamin absorption. However need for radiolabelled cobalamin, cumbersome method and limited usefulness in renal failure, has made it impractical at present.

(ii) Cobasorb test: a promising functional test which measures vitamin B_{12} absorption by estimating the increase in holotranscobalamin with and without intrinsic factor administration. The test requires further evaluation before it can be incorporated into routine clinical use.

TREATMENT OF VITAMIN B_{12} DEFICIENCY

Conventionally, vitamin B_{12} deficiency has been treated by parenteral (intramuscular route) supplementation with cyanacobalamin. However growing evidence suggests that oral vitamin B_{12} may be as good an option, regardless of the cause of vitamin B_{12} deficiency (38). The recommended standard treatment for vitamin B_{12} deficiency is described below.

(i) Parenteral route

Intramuscular injection (over deltoid muscle)1000µg daily for one week ,followed by once a week for 8 weeks followed by a monthly maintenance dose of 1000µg, usually lifelong – especially in the case of pernicious anemia

(ii) Oral route

500µg daily for nutritional deficiency as well as food cobalamin malabsorption and 1000µg daily for pernicious anemia(28)

Rationale for oral vitamin B_{12} supplementation

- the main causes of cobalamin deficiency in the elderly are food-cobalamin malabsorption (50–70%) and pernicious anaemia (20–30%)

- between 1 and 5% of free cobalamin (or crystalline cobalamin) is absorbed along the entire intestine by passive diffusion(9)

Evidence for oral vitamin B_{12} supplementation

The various studies supporting oral vitamin B_{12} supplementation are listed below in table 5 (39),(40)

Table 5. Studies on efficacy of oral vitamin B_{12} supplementation

Study design	Study population(n)	Dose, duration of treatment	Results	Reference
Open prospective	Food cobalamin malabsorption n=10	650µg/day 3 months	Normalization of serum B12 -80% Clinical improvement-20% Mean increase in Hb-1.9g/dl Mean decrease in MCV-7.8fl No adverse events	(41)
Open prospective	Non pernicious anemia n=20	1000µg/day 1 week	Normalization of serum B12 -85% No adverse events	(42)
Open prospective	Food cobalamin malabsorption n=30	250-1000µg/day 1 month	Normalization of serum B12 -87% Mean increase in Hb-0.6g/dl Mean decrease in MCV-3fl Dose effect≥500µg/day No adverse events	(43)
Open prospective	Non pernicious anemia n=30	125-1000µg/day 1 week	Normalization of serum B12 in all patients with at least one dose of ≥250µg/day Dose effect≥500µg/day No adverse events	(44)
Open prospective	Pernicious anemia n=10	1000µg/day 3 months	Normalization of serum B12 -90% Clinical improvement-30% Mean increase in Hb-2.45g/dl Mean decrease in MCV-10.4fl No adverse events	(45)

Table 5

An evidence-based analysis by the Vitamin B_{12} Cochrane Group concluded that the efficacy of oral cobalamin therapy, with a dose between 1000 and 2000 micrograms given initially daily and then weekly, is comparable to parenteral vitamin B_{12} supplementation, based on review of two randomized control trials described below (46) in table 6.

Table 6. Clinical trials on oral versus intramuscular vitamin B_{12} supplementation

Study	Year	Randomization method	Number	Withdrawal	Intent to treat	Follow up
Kuzminski**(47)**	1998	Unclear Not blinded	38	5	No	4 months
Bolaman **(48)**	2003	Block randomization Not blinded	70	10	No	3 months

Table 6

However, it must be borne in mind that the effect of oral cobalamin treatment in patients presenting with severe neurological deficits has not been adequately studied till date. Therefore, parenteral cobalamin therapy remains recommended for these patients.(33)

MATERIALS AND METHOD

MATERIALS AND METHOD

Study setting

Department of Gastrointestinal sciences, Christian medical college, Vellore

Study period

November 2009 to November 2010

I. Comparison of efficacy of oral versus intramuscular vitamin B_{12} supplementation

Study design

Single centre prospective open label randomized intervention trial

Inclusion Criteria

All patients with documented vitamin B_{12} deficiency (serum vitamin B_{12} level <200pg/ml)

who consent for the study

Exclusion criteria

1. Age <18years
2. Pregnant individuals
3. Renal failure
4. Special cases where parenteral B_{12} supplementation is mandatory

   (eg: those patients with severe neurological deficits, intestinal failure etc)

5. Already taking vitamin B_{12} supplements

Definitions

(i) Vitamin B_{12} deficiency : serum vitamin B_{12} levels less than 200 pg/ml

(ii) Treatment response : improvement in symptoms or signs along with either of the following – post treatment serum vitamin B_{12} > 200 pg/ml or post treatment serum homocysteine levels less than 13µM/L

(iii) Pernicious anemia : evidence of destruction of gastric fundic mucosa and presence of auto antibodies such as anti parietal cell antibody and/or anti intrinsic factor antibody

(iv) Food cobalamin malabsorption : a syndrome characterized by the inability of the body to release cobalamin from food or intestinal transport proteins, particularly in the presence of hypochlorhydria,where the absorption of 'unbound' cobalamin is normal

(v) Vegetarian : total abstinence from nonvegetarian diet at least during the last 3 years

(vi) Significant Proton pump inhibitor(PPI)/Metformin/H_2 receptor antagonists (H_2RA) use : uninterrupted regular use for at least 6 months.

(vii) Celiac sprue : Marsh III or above changes on duodenal biopsy along with IgA anti tissue transglutaminase (anti TTG) seropositivity

(viii) Tropical sprue : intestinal mucosal disease characterized by malabsorption of two or more unrelated nutrient groups where other known causes of malabsorption have been excluded.

Sample size

For comparison of oral versus intramuscular treatment groups,

Formula : number of patients, $n = \frac{2\,Sp^2\,(z_1\text{-}\alpha/2 + z_1\text{-}\beta/2)}{\mu_d^2}$

where $Sp^2 = \frac{s_1^2 + s_2^2}{2}$

Sp-standard deviation of mean of two groups

S_1^2- standard deviation of group 1 (intramuscular)

S_2^2- standard deviation of group 2 (oral)

μ_d^2- mean difference between samples

α-significance level

1-β – power of the study

The values used for calculation were derived from a study comparing oral versus intramuscular vitamin B12 by Kuzminski and colleagues(47)

[s1-165,s2-595, μd-400, α-5%, 1-β-80%]

The calculated sample size, **n = 19** in each arm of the study

Outcome measures

Primary outcome

– normalization of serum vitamin B12 levels after treatment

Secondary outcome

–clinical: improvement in symptoms and signs after treatment

- lab: change in Haemoglobin and MCV after treatment

- compliance with either forms of therapy

The study was approved by the ethics committee and the institutional review board of Christian Medical College, Vellore.

Data was collected by the principal investigator using a standard proforma (annexure1) after obtaining informed consent.

All the patients found to have vitamin B_{12} deficiency underwent a comprehensive etiological evaluation and those who consented for the clinical trial were randomly assigned to oral or intramuscular treatment groups in a 1:1 ratio. The randomization schedule was computer generated with concealed allocation and was prepared by someone uninvolved in the study. As the primary outcome measures were objective laboratory test reports, the use of placebo was not considered.

The etiological evaluation included complete blood counts, pernicious anemia antibody screening, IgG anti TTG estimation, HIV serology, stool examination for parasites, endoscopic mucosal biopsy from fundus and antrum of the stomach, duodenum as well as ileum, abdominal imaging with either a contrast enhanced CT scan or a combination of ultrasound and barium meal follow through, as well as urine or blood xylose estimation to assess mucosal malabsorption.

The study subjects in the oral group received 1000µg methylcobalamin tablets daily and those in the intramuscular group received 1000µg methylcobalamin over deltoid region daily for the first week of treatment followed by weekly injections for 8 weeks and monthly injections subsequently till review. The patients were followed up during the hospital visit after completion of 3 months of treatment and clinical as well as laboratory parameters were reviewed. Compliance was assessed by patient's account as well as pill / ampoule count and injection records where available.

II. Determination of intracellular vitamin B_{12} deficiency in patients with low normal serum vitamin B_{12} levels using serum homocysteine as a surrogate marker

Study design

Cross sectional observation study

Inclusion criteria

All patients with a serum vitamin B_{12} level less than 400pg/ml who consent for the study

Exclusion criteria

1. Age <18years
2. Serum creatinine >1.4mg/dl
3. Folic acid deficiency (serum folate <3ng/ml)
4. Pregnancy
5. Smoking or alcohol abuse
6. Levodopa therapy
7. Familial hyperhomocysteinemia

Definitions

(i) Low normal / Borderline vitamin B_{12} : serum vitamin B_{12} levels between 200 to 400 pg/ml

(ii) Hyperhomocysteinemia : serum total homocysteine levels more than 13 μM /L

Sample size

For determination of sample size, values were derived from studies by Yao et al (49) and Delva et al (50).

Using nMaster software, estimated sample size, **n=40**

Where [sensitivity of serum homocysteine (new test)-96%, sensitivity of serum vitamin B_{12} (reference test)-80%, α- 5%, 1-β -80%]

The study was approved by the ethics committee and the institutional review board of Christian Medical College, Vellore

Data was collected by the principal investigator using a standard proforma (annexure1) after obtaining informed consent.

Measurement

Serum vitamin B_{12} was estimated by electrochemiluminescence immunoassay (ECLIA) method (normal>200pg/ml) and high performance liquid chromatography (HPLC) method was used for serum homocysteine estimation (normal<13μM)

STATISTICAL METHODS

Data was analysed using SPSS software version 16.0. Continuous data is presented as mean with standard deviation and categorical data as proportions. Baseline characteristics were analyzed using Mann-Whitney U test for continuous variables and Fisher's exact test for categorical data. For the comparison of oral and intramuscular treatment groups, an intention to treat analysis was performed, assuming a negative treatment response for the patients who did not complete the study. A per protocol analysis was also done. In addition to descriptive statistics, Spearman's correlation was used to analyze the relationship between vitamin B_{12} and homocysteine.

RESULTS

RESULTS

The study analysed multiple aspects of vitamin B_{12} deficiency such as

(i) Comparison of efficacy of oral versus parenteral vitamin B_{12} supplementation

(ii) Etiology of vitamin B_{12} deficiency in tertiary care setting

(iii) Correlation between serum vitamin B_{12} and serum homocysteine (a marker of intracellular vitamin B_{12} function) in patients with low normal serum vitamin B_{12} levels

The results are discussed below separately.

I. Randomized trial of oral versus intramuscular vitamin B_{12} supplementation

72 patients were found to have vitamin B_{12} deficiency, of which 60 subjects who consented for the therapeutic trial were randomized to oral and intramuscular treatment groups in a 1:1 ratio. 27 patients in the intramuscular group and 22 patients in the oral group completed the study, as described in figure 3 below.

Figure 3. Randomized trial of oral versus intramuscular vitamin B_{12} supplementation

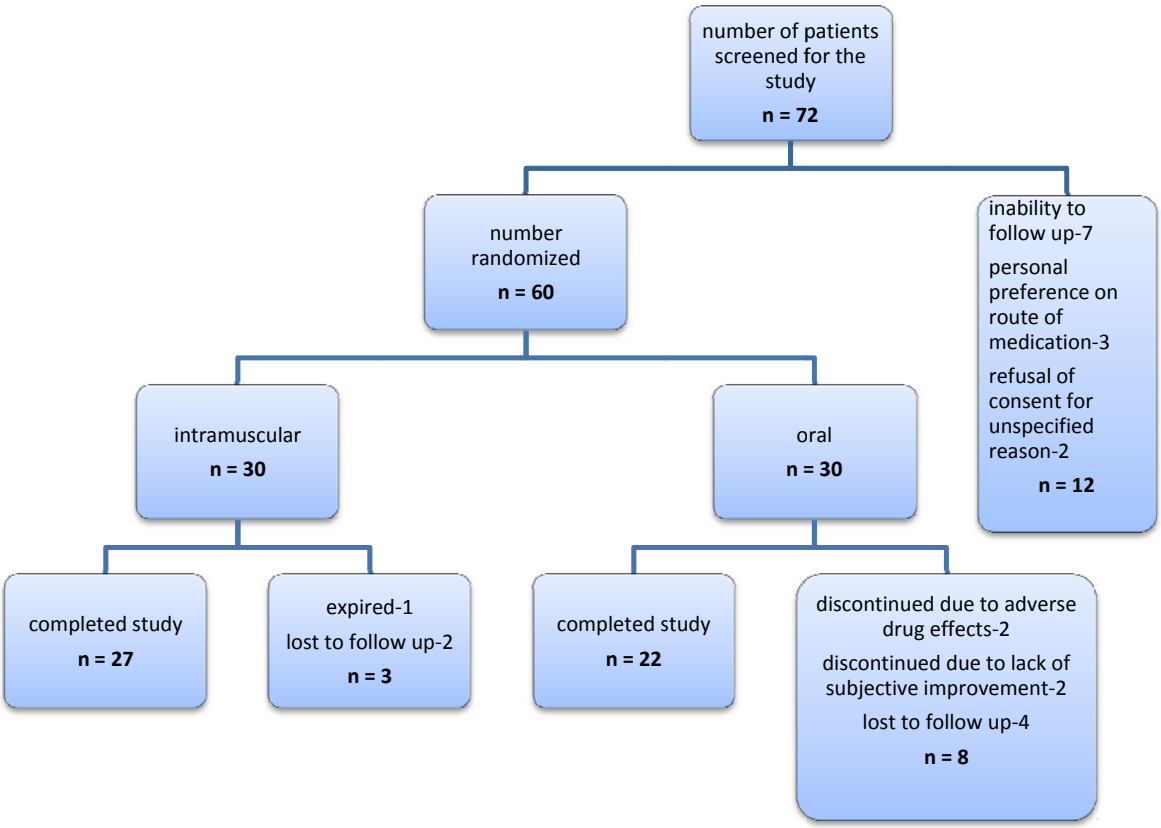


Figure 3

Baseline characteristics

The baseline characteristics of both the study groups are illustrated below in table 7

Table 7. Baseline characteristics of oral and intramuscular treatment groups

Characteristics	Intramuscular	Oral	P value
Number of patients, n	30	30	-
Male gender (n,%)	25 (83.3%)	19 (63.3%)	0.14
Mean age (years)	44.3±9.3	38.6±14.8	0.06
Clinical features			
Diarrhea	19	11	0.07
Anorexia	11	18	0.12
Skin hyperpigmentation	2	4	0.67
Neurological features	4	1	0.35
Pallor	6	7	0.76
No symptoms/signs	5	7	0.75
Comorbidities			
Diabetes	2	4	0.67
Hypertension	3	6	0.47
Cause of B_{12} deficiency			
Pernicious anemia	7	6	1.00
Atrophic gastritis	6	6	1.00
Celiac sprue	2	2	1.00
Tropical sprue/enteropathy	1	4	0.35
Vegetarian diet	1	3	0.61
Ileal resection	1	1	1.00
Multiple causes	8	4	0.30
No cause identified	4	4	1.00
H.pylori infection	20	17	0.60
APCA	10	10	1.0
Anti IF	5	2	0.42
IgA anti TTG	7	6	1.00
Pre-treatment Hb (g/dl)	12.4±2.7	11.7±2.4	0.17
Pre-treatment MCV (fl)	89.4±16.3	92.8±14.3	0.37
Pre-treatment serum vitamin B_{12}(pg/ml)	146.0±42.1	149.8±37.6	0.82

There were 30 patients each in the oral and intramuscular treatment groups. The distribution of baseline characteristics such as age-sex distribution, clinical features, laboratory parameters, etiology as well as risk factors of both the study groups were similar (table 7). The most common cause of vitamin B_{12} deficiency was pernicious anemia in both the study groups.

Treatment response

All the 27 patients who completed intramuscular treatment and 20 out of the 22 patients who completed oral therapy, achieved normalization of serum vitamin B_{12} levels (table 8).

Table 8. Post treatment serum vitamin B_{12} levels

Post treatment serum Vitamin B_{12} (pg/ml)	Intramuscular (n=27)	Oral (n=22)
<200	Nil	2
200-300	2	2
>300	25	18

The intention to treat analysis, assuming lack of treatment response for the patients who did not complete the study showed no difference in treatment responses between the oral and intramuscular treatment groups (p=0.06).

Similar finding was observed in per protocol analysis as well (p=0.2).

The post treatment parameters of both the study groups are listed below (table 9).

Table 9. Comparison of post treatment parameters

Test	Intramuscular	Oral	p value
Serum vitamin B_{12} (pg/ml)	1128.3±543.0	488.4±173.1	<0.01
Hb (g/dl)	13.4±2.2	12.8±2.0	0.45
MCV(fl)	86.5±8.1	87.3±8.1	>0.05

There was no significant difference in the increase in haemoglobin (Hb) levels or decrease in mean corpuscular volume (MCV) between the oral and intramuscular treatment groups. The increase in serum vitamin B_{12} levels after treatment was higher in patients who received intramuscular treatment, compared to those who were on oral therapy (mean change 982.3 vs 338.6 pg/ml respectively, $p<0.01$).

Serum homocysteine levels before and after treatment were available for 3 patients in intramuscular group and 7 patients in the oral treatment group. The post treatment levels were much lower than the pre-treatment values in all these patients.

Among patients who received oral treatment, there was no difference in treatment response between patients who had pernicious anaemia compared to those who had vitamin B_{12} deficiency due to other causes ($p=0.37$)

Compliance

All the patients (from oral as well as intramuscular treatment groups) who completed the study reported ≥80% compliance to treatment.

Cost analysis (for 3 months of treatment)

❖ Cost of oral vitamin B_{12} supplementation

= cost of 1000µg methylcobalamin(daily dose) x duration of treatment

= Rs 12.50 x 90

= **Rs 1125.00**

❖ Cost of intramuscular vitamin B_{12} supplementation

= (cost of 1000µg methylcobalamin + disposable syringe and needle + injection charges)

x number of doses for 3 months

= Rs (190.8 + 5.0 + 30) x 16

= **Rs 3612.80**

II. Etiology of vitamin B_{12} deficiency

Complete etiological evaluation was done for the 72 patients detected to have vitamin B_{12} deficiency who were screened for the randomized trial. The various causes identified are listed below (table 10)

Table 10. Causes of vitamin B_{12} deficiency

Cause	Number of patients(n=72)	%
Pernicious anaemia	17	24
Atrophic gastritis-H pylori related **Non H pylori related**	13 2	18 2
Tropical sprue/enteropathy	5	7
Celiac sprue	4	6
Vegetarian diet	4	6
Ileal resection	2	2
Multiple causes*	17	24
No cause identified	8	11

*included those causes listed above as well as other causes such as PPI/H_2RA/Metformin use, pancreatic exocrine insufficiency, persistent giardiasis with malabsorption etc

The most common cause of vitamin B_{12} deficiency in the study population was pernicious anaemia, followed by atrophic gastritis (involving fundus of stomach). More than one cause existed in 24% patients, which included pancreatic exocrine insufficiency, chronic use of metformin/proton pump inhibitor/H_2 receptor antagonists and parasitic infestation such as refractory giardiasis. No cause was identified for 8 out of 72 study subjects (11%).

III. Correlation between serum vitamin B_{12} and homocysteine

For the analysis of correlation between serum vitamin B_{12} and homocysteine levels, 97 patients (61 male, 37 female) with serum vitamin B_{12} levels less than 400pg/ml were enrolled.

47 patients had serum vitamin B_{12} levels less than 200pg/ml and 50 had serum vitamin B_{12} in 200-400pg/ml range.

Characteristics of the study population

Table 11 illustrates the distribution of baseline characteristics of the study population (n=97).

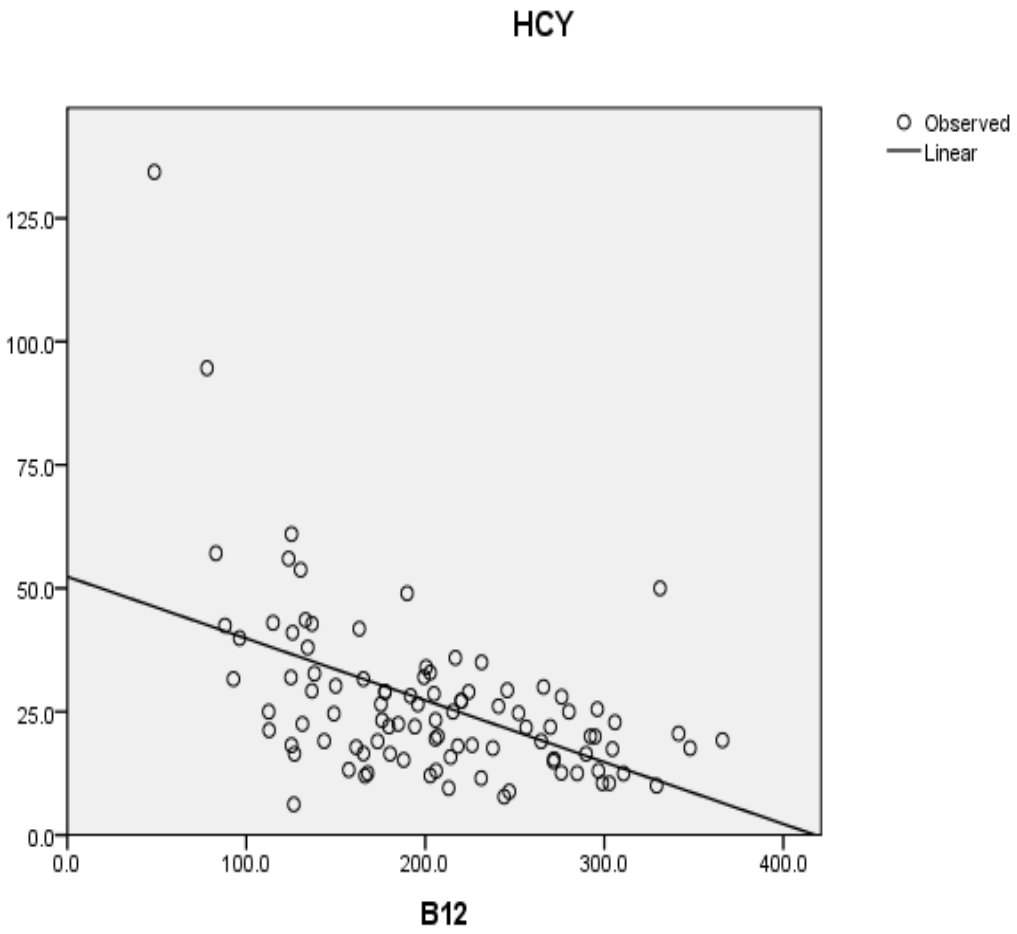
Table 11. Patient characteristics

Male gender	**61 (63%)**
Age (years)	**40.9±13.0**
Hb (g/dl)	**12.3±2.3**
MCV(fl)	**88.1±12.7**
Serum homocysteine (µM)	**26.8±17.5**
Serum Vitamin B_{12}(pg/ml)	**203.9±70.0**

Correlation between vitamin B_{12} and homocysteine

The correlation between serum vitamin B12 (0-400pg/ml range) and homocysteine is demonstrated below (figure 4)

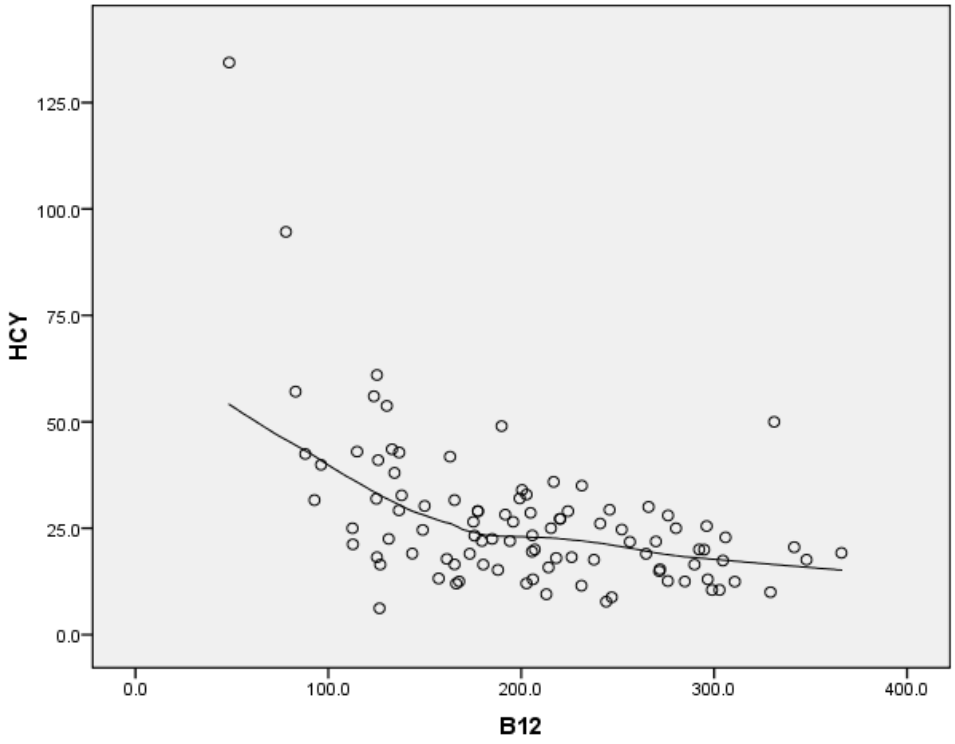
Figure 4. Correlation between serum vitamin B_{12} and serum homocysteine



There was a significant inverse correlation between serum vitamin B12 and homocysteine levels (Spearman correlation coefficient, $r = -0.47$, $p<0.01$)

On further analysis using a Loess curve, it was found that though there was a strong inverse correlation between serum vitamin B_{12} and serum homocysteine levels in patients with vitamin B_{12} deficiency, ie serum vitamin B_{12} <200 pg/ml (Spearman correlation coefficient, r = -0.44, p<0.01), the same was not true for the patients with low normal serum vitamin B_{12} levels, ie 200-400 pg/ml ((Spearman correlation coefficient, r = -0.22, p=0.11). This is demonstrated in the figure below (figure 5)

Figure 5. Loess curve showing difference in correlation of serum vitamin B_{12} <200pg/ml and 200-400pg/ml with serum homocysteine



Cellular deficiency of vitamin B_{12} in patients with low normal serum vitamin B_{12}

50 patients with a serum vitamin B_{12} level in the low normal range of 200-400pg/ml were analysed to find out whether they have a cellular deficiency of vitamin B_{12}, using serum homocysteine as a surrogate marker.

37 patients (74%) had elevated serum homocysteine levels suggestive of vitamin B_{12} deficiency at cellular level.

Risk factors for vitamin B_{12} deficiency (figure 6) such as long term metformin or proton pump inhibitor use, vegetarian diet etc were more common in patients who had hyperhomocysteinemia

The clinical features suggestive of cobalamin deficiency (figure 7) were more common in patients with elevated homocysteine levels, consistent with inadequate intracellular function of vitamin B_{12}

Figure 6

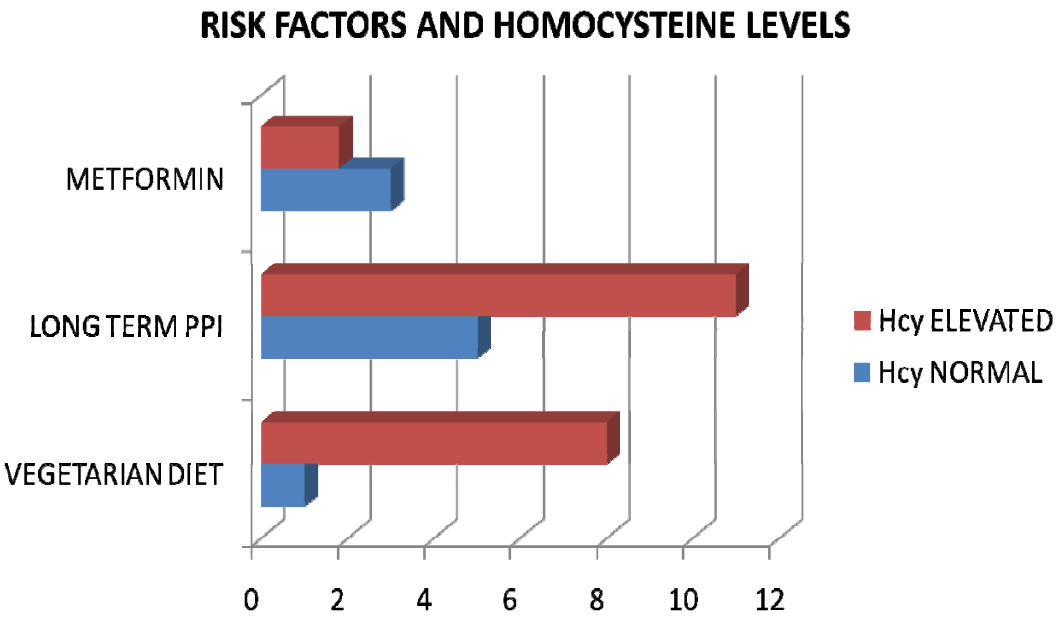
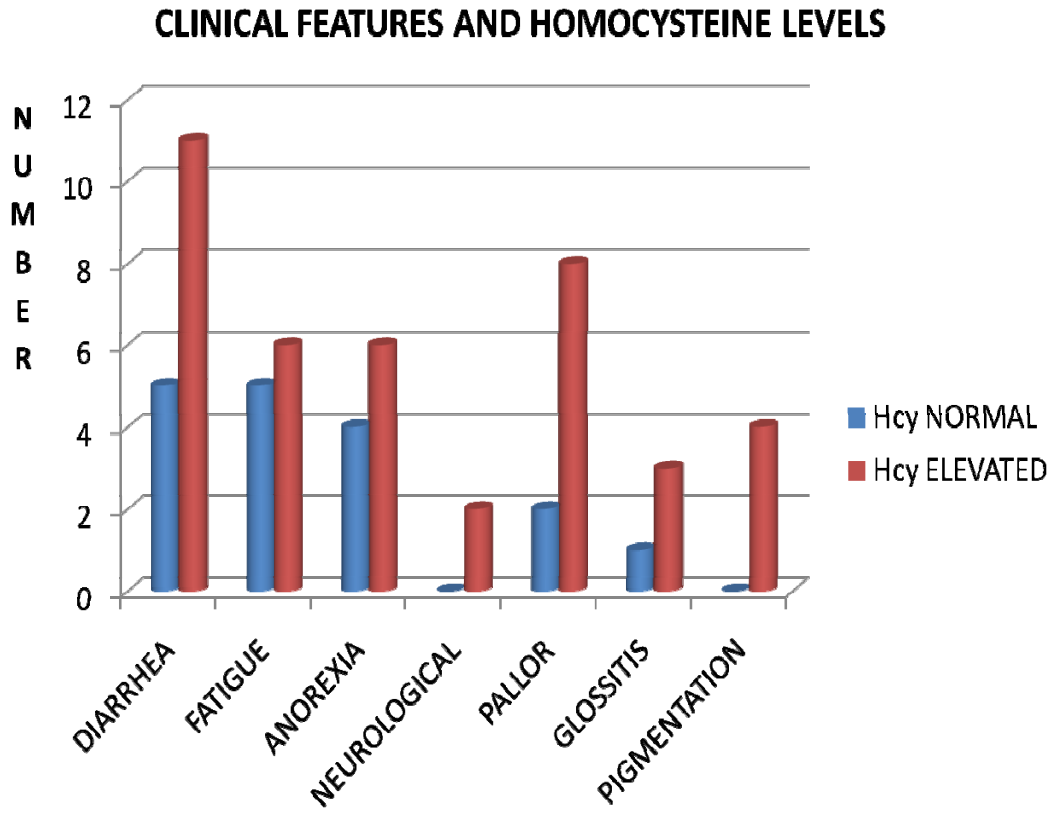
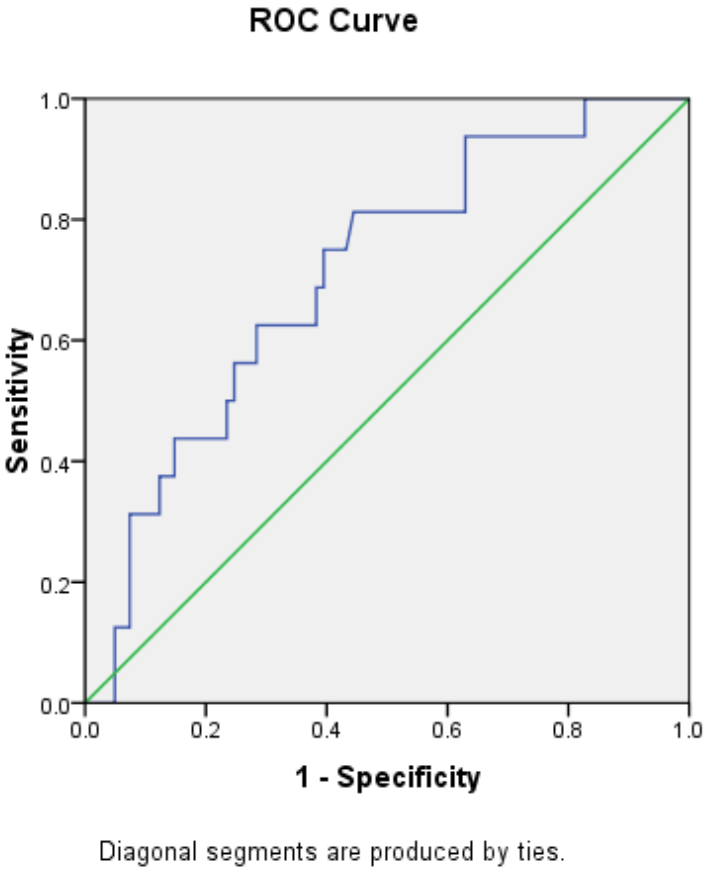


Figure 7



Using receiver operating characteristic (ROC) curve method, the currently recommended lower limit of normal serum vitamin B_{12} level (200 pg/ml) was found to have a sensitivity of only 81.2% for the diagnosis of intracellular vitamin B_{12} deficiency, using serum homocysteine levels as a surrogate marker.

Figure 7. ROC curve using serum vitamin B_{12} and serum homocysteine levels



DISCUSSION

DISCUSSION

Studies on rural and urban population in western India have demonstrated a higher prevalence of vitamin B_{12} deficiency compared to western countries and established its association with hyperhomocysteinemia, which is a known cardiovascular risk factor (14)(1). However, not much is known about the causes of vitamin B_{12} deficiency in the Indian setting.

Eventhough the vast majority of patients with vitamin B_{12} deficiency are in subclinical stage and do not have classically described clinical manifestations, at least some of them may be at an increased risk for developing serious clinical consequences if not detected and treated early. The treatment is safe and remarkably efficacious if initiated before permanent clinical sequelae occur.

The detection of vitamin B_{12} deficiency is hampered by the poor ability of serum vitamin B_{12} estimation to reflect cellular deficiency of the vitamin in the low normal/borderline range (2)(25). The above suggests that there is an imminent need for developing a reliable technique for the detection of cellular deficiency of vitamin B_{12} . Given the high prevalence of vitamin B_{12} in our population, it is also important to evolve a cost effective strategy for its treatment.

The present study determined the etiology of vitamin B_{12} deficiency in a tertiary care setting, compared the efficacy of oral versus parenteral vitamin B_{12} supplementation in patients with vitamin B_{12} deficiency, examined the correlation of serum levels of vitamin B_{12} and homocysteine, and looked into the presence of cellular deficiency of vitamin B_{12} in patients with low normal serum vitamin B_{12} using serum homocysteine as the surrogate marker. To our knowledge this is the first study of its kind from the Indian subcontinent.

The data available from previous small studies suggest equal efficacy of high dose oral and parenteral modes of vitamin B_{12} supplementation (table 5, 6). However, data from tropical countries are lacking, and given the difference in gut characteristics in terms of intestinal mucosal morphology, composition of intestinal microbiota and a high prevalence of parasitic infestations, the extrapolation of the western data to our population is questionable.

The present study confirms that oral vitamin B_{12} supplementation is as effective as intramuscular treatment in the normalization of serum vitamin B_{12} levels in patients with vitamin B_{12} deficiency. The improvements in other clinical and laboratory parameters (such as haemoglobin, mean corpuscular volume and serum homocysteine) were also found to be similar between the two study groups. The patients showed good compliance to both forms of treatment. However the intramuscular vitamin B_{12} supplementation was three times more expensive compared to the oral therapy and did not seem to confer any significant advantages over oral vitamin B_{12} supplementation.

The study also revealed that the response to oral treatment did not differ between patients with vitamin B_{12} deficiency due to pernicious anaemia and those with vitamin B_{12} deficiency due to other causes. This finding suggests that oral vitamin B_{12} supplementation may be effective regardless of the cause of vitamin B_{12} deficiency.

The majority of patients (74%) with borderline serum vitamin B_{12} levels (200-400pg/ml) was found have hyperhomocysteinemia, suggestive of vitamin B_{12} deficiency at cellular level. The finding substantiates the usefulness of serum homocysteine as an ancillary test to guide treatment in patients with low normal serum vitamin B_{12} levels.

We found that a strong inverse correlation exists between serum vitamin B_{12} and serum homocysteine levels in patients with vitamin B_{12} deficiency, consistent with the previous studies by Fakhrzadeh et al and Refsum et al(14)(37). However, a similar correlation was not found in patients with low normal/borderline serum vitamin B_{12} levels. This may be partially explained by the poor reliability and high intraindividual variation of serum vitamin B_{12} estimation in low normal/borderline range (200-400pg/ml) (34). Preliminary studies have reported that plasma holotranscobalamin estimation may be a better indicator of vitamin B_{12} deficiency as it measures the metabolically active form of vitamin B_{12} rather than the total serum vitamin B_{12} levels(51). Further studies are needed to identify a cheap, widely available, highly sensitive and specific serum biomarker which accurately reflects the intracellular deficiency of vitamin B_{12}.

Using the ROC curve method, it was found that the current serum vitamin B_{12} level cut off of 200pg/ml fails to identify about 19% of patients with intracellular vitamin B_{12} deficiency. Large correlational studies between serum vitamin B_{12} and the novel serum biomarkers of vitamin B_{12} deficiency are needed to redefine the best cut off value for the lower limit of normal serum vitamin B_{12} levels.

The study also throws light into the etiology of vitamin B_{12} deficiency in a tertiary care setting in India. Pernicious anemia, followed by atrophic gastritis involving gastric fundus were the most common causes. This finding is similar to the data previously reported from the western countries. Importantly, a number of treatable causes like celiac sprue, tropical sprue etc were identified. The cause of vitamin B_{12} deficiency could be successfully elucidated in 89% of the patients with the combination of endoscopic and laboratory investigations used in the study, even without the use of Schilling's test.

There were a few limitations for our study such as small size of study population and short follow up period. The correlation between serum vitamin B_{12} and serum homocysteine at serum vitamin B_{12} levels >400pg/ml has not been addressed. Concurrent estimation of methyl malonic acid would have allowed a more specific diagnosis of cellular deficiency of vitamin B_{12}.

CONCLUSIONS

CONCLUSIONS

- Oral vitamin B_{12} supplementation is cheaper and equally effective as intramuscular treatment for vitamin B_{12} deficiency.

- A majority of patients with borderline serum vitamin B_{12} levels (200-400pg/ml) have hyperhomocysteinemia, suggestive of vitamin B_{12} deficiency at cellular level.

- Serum homocysteine is a useful ancillary test for the diagnosis of intracellular vitamin B_{12} deficiency in patients with low normal/borderline serum vitamin B_{12} levels.

- The most common etiology for vitamin B_{12} deficiency in a tertiary care hospital setting in India is pernicious anemia, followed by atrophic gastritis involving fundus of stomach.

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B12 STUDY-PROFORMA

NAME: AGE: yrs SEX: M/F Serial No:

Address: Hospital No:

Phone : Occupation:

E mail:

FINAL DIAGNOSIS (CAUSE OF B12 DEFICIENCY):

PRESENTING COMPLAINTS:

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1) Memory loss: Y/N
2) Parasthesia: Y/N
3) Motor weakness: Y/N
4) Ataxia: Y/N
5) Psychiatric symptoms: Y/N
6) Skin darkening: Y/N
7) Fatigue/malaise: Y/N
8) Diarrhea: Y/N
9) Anorexia: Y/N

PAST AND TREATMENT HISTORY:

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1) Diabetes mellitus: Y/N. Duration:
2) Hypertension : Y/N. Duration :
3) IHD: Y/N. Duration:
4) Dyslipidemia: Y/N
5) CVA in past: Y/N
6) Drug history: PPIs- Y/N duration : mon

   H2RAs- Y/N duration : mon

   METFORMIN- Y/N duration : mon
7) Smoking: Y/N
8) Alcohol: Y/N Qty: Duration: Last intake:
9) Diet: veg/ non-veg /vegan
10) GI surgery: Y/N Ind: Procedure:

    Year:
11) Occupational exposure: Nitrous oxide Y/N

    Other toxins Y/N

EXAMINATION:

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1) pallor: Y/N
2) glossitis: Y/N
3) oral ulcers Y/N
4) pedal edema: Y/N
5) skin hyperpigmentation: Y/N

6) RS:

7) CVS:

8) P/A:

9) CNS: optic neuritis/ atrophy:

Peripheral neuropathy:

Myelopathy:

Hemiplegia:

UMN facial palsy:

Plantar:

Ataxia/ post column signs:

Cerebellar signs:

Pyramidal signs:

10**)** **<u>MMSE:</u>**

1) date: (year)(season)(date)(day)(month) - **__/5** points

2) Where are we: (state)(county)(town)(hospital)(floor) - **__/5** points

3) Name three objects: one second to say each. Ask the patient all three after you have said them. Give one point for each correct answer. Then repeat them until he/she learns all three. Maximum score - **__/3** points.

4) Serial 7s, beginning with 100 and counting backward: one point for each correct; stop after five answers. Alternatively, spell WORLD backwards: one point for each letter that is in correct order. Maximum score - __/**5** points.

5) Ask for the three objects repeated above: one point for each correct. Maximum score - __/**3** points

6) Show and ask patient to name a pencil and wrist watch - __/**2** points

7) Repeat the following, "No ifs ands or buts." Allow only one trial - _/**1** point

8) Follow a three stage command, "Take a paper in your right hand, fold it in half, and put it on the floor." Score one point for each task executed. Maximum score - __/**3** points

9) On a blank piece of paper write "close your eyes," and ask the patient to read and do what it says - __/**1** point

10) Give the patient a blank piece of paper and ask him/her to write a sentence. The sentence must contain a noun and verb and be sensible. Ask him to copy a intersecting pentagon- __/**2** points

TOTAL MMSE: __/30

LAB PARAMETERS:

1) HB: TC: PLT: RETICS:

2) MCV:

3) PERIPHERAL SMEAR:

4) T.B/D.B: AG RATIO: LDH:

5) VITAMIN B12: FOLATE:

6) TSH:

7) URINE D-XYLOSE

8) HIV ELISA:

9)ANTI PARIETAL CELL Ab - **anti IF –**

10)ANTI TTG +/-

11) STOOL PARASITES- **OCCULT BLOOD-**

12)SERUM HOMOCYSTEINE

OTHER RELEVANT INVESTIGATIONS:

IMAGING STUDIES

A.USG/CECT ABDOMEN:

B.BMFT:

ENDOSCOPIC EVALUATION

A.GASTROSCOPY:

B.COLONOSCOPY:

HISTOPATHOLOGY:

A.STOMACH:

B.DUODENUM:

C.ILEUM:

FOLLOW UP VISIT (after 3 months)

1) SYMPTOMS – IMPROVED/ NO CHANGE/ WORSENED

2) FINDINGS – IMPROVED/ NO CHANGE/ WORSENED

3)LABORATORY INVESTIGATIONS - Hb MCV

- VITAMIN B 12

- OTHER

4)COMPLIANCE

INFORMED CONSENT

I understand that department of Gastrointestinal sciences, Christian Medical College, Vellore is doing a study to

(i) identify the etiological factors of vitamin B12 deficiency

(ii)compare the efficacy of oral versus parenteral vitamin B12 supplementation in subjects with deficiency of the vitamin, and

(iii) evaluate whether serum homocysteine levels can be used as a surrogate marker of intracellular deficiency of vitamin B12 in patients with low normal serum Vitamin B12 levels

The study involves collection of patient information, clinical data and test reports done as part of regular clinical care. I also understand that some of the tests done in connection with the study may directly benefit me whereas the other tests are likely to benefit other patients with the disease.

I understand that I may receive either oral or intramuscular vitamin B12 as treatment and have been informed that either route of administration is equally efficacious according to the available scientific evidence at present.

I understand that my withdrawal from the study, at any time will not affect the treatment being given.

Study Title: **COMPARISON OF EFFICACY OF ORAL VERSUS INTRAMUSCULAR VITAMIN B_{12} SUPPLEMENTATION FOR TREATMENT OF VITAMIN B_{12} DEFICIENCY AND DETERMINATION OF CELLULAR DEFICIENCY OF VITAMIN B_{12} USING SERUM HOMOCYSTEINE AS A SURROGATE MARKER IN PATIENTS WITH LOW NORMAL SERUM VITAMIN B_{12} LEVELS**

Study Number:

Subject's Initials: _____ Subject's Name: _____

Date of Birth / Age:_____

Please initial box

(Subject)

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am

free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission

to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s) [ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative:_____

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature of the Witness: _____

Date:_____/_____/_____

Name of the Witness: _____

KEY TO MASTERCHART

I. B12 TRIAL –ORAL VS INTRAMUSCULAR TREATMENT (masterchart 1)

- R No – random allocation number [arranged by category –intramuscular, followed by oral, and then followed by patients who were screened for trial, but excluded(X1-X12) for various reasons and considered only for etiological evluation]
- HOS NO – hospital number
- G – gender
- A - age
- State
    - TN – tamil nadu
    - WB – west bengal
    - AP – andhra pradesh
    - JHA – jharkhand
    - KAR – karnataka
    - MEGHA – meghalaya
    - TRIPU – tripura
    - CHAT - chattisgarh
- CAT- Category
    - 1 : intramuscular treatment group
    - 2 : oral treatment group
    - 3 : screened, but excluded from the trial (considered only for etiology)
- DX- Diagnosis
    - 0 : no cause identified
    - 1 : pernicious anaemia
    - 2 : caeliac sprue
    - 3 : tropical sprue/enteropathy
    - 4 : inflammatory bowel disease (A-Crohns disease, B-ulcerative colitis)
    - 5 : vegetarian diet
    - 6 : drug (A-PPI,B-H_2RA,C-METFORMIN)

    - 7 : atrophic gastritis (A- Hpylori related, B- Non Hpylori related)
    - 8 : pancreatic exocrine insufficiency
    - 9 : ileal surgery
- S – symptoms (1=present,2=absent)
- S1 – memory disturbances (1=present,2=absent)
- S2 – parasthesias (1=present,2=absent)
- S3 – psychiatric disturbances (1=present,2=absent)
- S4 – skin hyperpigmentation (1=present,2=absent)
- S5 – fatigue/malaise (1=present,2=absent)
- S6 – diarrhea (1=present,2=absent)
- S7 – anorexia (1=present,2=absent)
- DM – diabetes mellitus (1=present,2=absent)
- HT – hypertension (1=present,2=absent)
- IHD – ischaemic heart disease
- DL – dyslipidemia (1=present,2=absent)
- CV – cerebrovascular accident (1=present,2=absent)
- D1 – proton pump inhibitor use (1=present,2=absent)
- D2 – metformin use (1=present,2=absent)
- SM- smoking (1=present,2=absent)
- AL-alcohol abuse(1=present,2=absent)
- DE- diet (1-vegetarian,2-nonvegetarian)
- SX – ileal surgery
- F1 – pallor (1=present,2=absent)
- F2 - glossitis (1=present,2=absent)
- F3 – oral ulcers (1=present,2=absent)
- F4 – neurological findings (1=present,2=absent)
- HB1- pretreatment haemoglobin(g/dl)
- HB2 – posttreatment haemoglobin(g/dl)
- MC1 – pretreatment mean corpuscular volume(fl)
- MC2 – posttreatment mean corpuscular volume(fl)
- B12A - pretreatment serum vitamin B12(pg/ml)
- B12B - posttreatment serum vitamin B12(pg/ml)

- HC1 – pretreatment serum homocysteine (μM/L)
- HC2 – posttreatment serum homocysteine (μM/L)
- RX – treatment response (1=responded, 2=not responded)
- AP – antiparietal cell antibody (1=present,2=absent)
- IF – antiintrinsic factor antibody (1=present,2=absent)
- TTG– anti tissue transglutaminase antibody (1=present,2=absent)
- SP- stool parasites(1=present,2=absent)
- HPA – histopathology of antrum, HPF- histopathology of fundus (stomach)
    - 1- normal
    - 2- chronic atrophic gastritis, Hpylori related
    - 3- chronic atrophic gastritis, non Hpylori related
    - 4- autoimmune gastritis
    - 5- other
- HPD – histopathology of duodenum, HPI – histopathology of ileum
    - N- normal
    - X – data not available
- HP – Helicobacter pylori (1=present,2=absent)
- SUB – subjective improvement (1=improved, 2=worsened, 3=no change)
- COM – compliance (%)

II. VITAMIN B12 – HOMOCYSTEINE CORRELATION (masterchart 2)

- H No – Hospital number
- State
    - TN – tamil nadu
    - WB – west bengal
    - AP – andhra pradesh
    - JHA – jharkhand
    - KAR – karnataka
    - ORI – orissa
    - MEGHA – meghalaya
    - TRIPU – tripura
    - CHAT - chattisgarh
    - BAN - bangladesh
- HB – haemoglobin (g/dl)
- MCV – mean corpuscular volume (fl)
- B12 – serum vitamin B12 (pg/ml)
- HCY – serum homocysteine (μM/L)
- PSY – psychiatric symptoms (1=present,2=absent)
- SKI – skin hyperpigmentation (1=present,2=absent)
- MAL – fatigue/malaise (1=present,2=absent)
- DIA – diarrhea (1=present,2=absent)
- AX – anorexia (1=present,2=absent)
- H2R – H2 receptor antagonist use (1=present, 2=absent)
- MET – metformin use (1=present,2=absent)
- DIET - (1=vegetarian,2=non vegetarian)
- SUR- ileal surgery (1=yes,2=no)
- PAL – pallor (1=present,2=absent)
- GL – glossitis (1=present,2=absent)
- OR – oral ulcers (1=present,2=absent)
- STOMACH/DUODENAL HISTOLOGY (X –data not available)

R N	NAME	HOS NO	G	A	STATE	CAT	DX	S	S1	S2	S3	S4	S5	S6	S7	DM	HT	IHD	DL	CV	D1	D2	SM	AL	DE	SX	F1	F2	F3	F4	HB1	HB2	MC1	MC2	B12A	B12B	HC1	HC2	RX	AP	IF	SP	TTG	HPA	HPF	HPD	HPI	HP	SUB	COM
1	KRISHNA PRASAD RAJA	575993D	M	44	KERALA	1	1,5	1	2	2	2	2	1	2	1	2	2	2	2	2	2	2	1	2	1	2	2	2	2	2	13.1	13.3	88	86.2	157.2	1005	13.2	X	1	2	1	2	1	3	3	N	X	2	1	100
3	BASANTH MAHTO	589418D	M	47	JHA	1	7A	1	2	2	2	2	1	2	1	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	6.1	6.9	81.6	90.9	197.7	1495	X	5.9	1	2	2	1	2	2	2	MILD CHRONIC DUODENITIS	X	1	1	100
8	SANKAR KUMAR GHOSH	316650D	M	57	WB	1	7A	1	2	2	2	2	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	12.3	14.1	93.1	94.7	189	1284	X	21	1	1	2	2	2	2	2	N	N	1	1	100
9	SULEKHA DEY	610095D	F	44	ASSAM	1	7A	1	2	2	2	2	1	1	1	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	9.8	8.4	59.7	59	124.9	381.4	31.9	X	1	2	2	2	1	2	2	N	X	1	3	80
10	SEKAR J	576351D	M	42	AP	1	5,7A	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	15.5	15	94.5	93.2	131.3	772.3	22.5	15.4	1	2	2	2	2	2	2	N	N	1	3	100
12	RAGHUNATH REDDY	609122D	M	43	AP	1	2,7A	1	2	1	2	1	1	1	1	2	2	2	2	2	2	2	1	1	2	2	1	2	2	1	6.6	15.4	129	X	78.01	680.5	94.6	X	1	2	2	2	1	2	2	MILD VILLOUS ATROPHY	N	1	1	100
15	ANUGRAH N SINGH	618868D	M	51	JHA	1	2	1	2	2	2	2	1	1	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	9.9	13.5	110	87.8	88.04	293.4	42.5	X	1	2	2	2	2	3	3	SUBTOTAL VILLOUS ATROPHY	N	2	1	100
16	ANTAKA TAMANG	617252D	F	38	WB	1	1,6A	1	2	2	2	2	2	1	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	12.1	12.2	89.3	85.7	194.1	843.3	22		1	1	2	2	2	2	2	MILD CHRONIC DUODENITIS	N	1	1	100
17	SURESH KUMAR PATEL	437690D	M	43	MP	1	7A	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	1	2	2	2	2	2	2	13.1	X	94.4	X	187.9	X	15.2	X	2	2	2	2	2	2	2	N	N	1	X	X
18	MENUKA DANGAL	627493D	F	43	NEPAL	1	0	1	2	1	2	2	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	13.1	13.1	98.8	94.2	197.4	1858	14	9.81	1	2	2	1	2	1	1	N	X	2	1	100
20	KATHIRVEL S	598782D	M	57	TN	1	5,6C	2	2	2	2	2	2	2	2	1	1	2	2	2	2	1	2	2	1	2	2	2	2	2	14.5	12.2	87.9	85.7	138	843.3	32.7	X	1	2	2	2	2	2	2	N	N	1	3	100
23	SUSANTHA MONDAL	647840B	M	42	WB	1	1	1	2	2	2	2	1	2	1	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	13.2	14	85.8	88.2	196	948.7	X	X	1	1	2	2	2	2	2	MILD CHRONIC DUODENITIS	MILD ACTIVE ILEITIS	1	3	100
25	PRABIR KUMAR ROY	653180D	M	44	WB	1	1	1	2	2	2	2	1	1	2	2	1	2	2	2	2	2	1	2	2	2	2	2	2	2	11.1	12.5	82.9	75.2	160.7	1577	59.7	X	1	2	1	2	2	2	5	N	N	1	1	100
26	SYED SHAID R	665073D	M	36	TN	1	3	1	2	2	2	2	1	1	2	2	2	2	2	2	2	2	1	1	2	2	2	2	2	2	14.9	18.3	118	100	97.55	209.6	X	X	1	1	2	2	2	2	1	INCREASED IEL,VILLOUS ATROPH	X	1	1	100
29	PRASAD AL	623593D	M	41	JHA	1	6B,7A	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	13.8	12.9	86.4	86.4	136.6	888.1	29.2	X	1	2	2	2	1	2	2	MILD CHRONIC DUODENITIS	N	1	1	100
33	ARUN KUMAR TANTI	391770D	M	42	JHA	1	0	1	2	2	1	2	2	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	12.4	14.1	91.4	78	96.2	860.4	39.9	X	1	2	2	2	1	1	1	N	N	2	1	100
34	ANJU DEVI	654619D	M	40	JHA	1	0	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	10.3	12.4	75	85	126.5	1029	16.2	X	1	2	2	2	1	1	1	N	N	2	1	100
35	RADHE SHYAM MANDAL	186959D	M	53	NEPAL	1	5	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	13.3	13.5	95.8	92.3	136.8	1420	25.5	X	1	2	2	2	2	2	1	N	N	1	1	90
36	CHINNA THAMBI	701111A	M	47	TN	1	1	1	2	2	2	2	1	2	2	2	2	2	2	2	2	2	1	2	2	2	1	2	2	2	8.9	13.1	62	X	140.2	1460	X	X	1	1	1	2	2	4	4	LYMPHANGEIECTASIS	N	2	1	100
41	PARIMALA	641784D	F	40	AP	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	8.4	13.1	70.8	85.7	86	340.5	X	9	1	1	1	2	2	4	1	X	X	2	3	100
42	BIPUL ROY	709948D	M	30	WB	1	0	1	2	2	2	2	2	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	14.1	14.9	88	87.6	189.8	930.6	49	X	1	2	2	2	2	2	1	N	N	1	1	100
44	DEBABRATA DEY	914627C	M	61	WB	1	2	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	11.2	11.7	119	93.6	179.5	2000	X	X	1	2	2	2	1	1	5	INCREASED IEL,VILLOUSATROPH	MILD CHRONIC ILEITIS	2	1	100
46	DHAMAYANTHI	702010D	M	39	TN	1	1	1	2	2	2	1	1	1	1	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	9	X	64.6	X	172.5	X	X	X	2	1	2	1	2	2	2	N	X	1	X	X
48	SAMPATH S	562950D	M	54	TN	1	6A,7A	1	2	1	2	2	1	2	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	14.6	X	89.5	X	170.3	X	X	X	2	2	2	2	2	2	2	MILD CHRONIC DUODENITIS	N	1	X	X
51	JAGADISH PRASAD SAH	717824D	M	65	JHA	1	7A	1	2	2	2	2	1	1	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	14	14.2	71.3	73	184.9	2000	22.5	X	1	2	2	2	2	2	2	N	N	1	1	100
52	BIKAS KUMAR SAHU	723577D	M	29	JHA	1	7A	1	2	2	2	2	2	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	14.5	14.1	92.6	88.3	166.5	2000	17.4	11.3	1	2	2	2	2	2	2	N	N	1	1	100
53	JOTHI LINGAM	293387D	M	50	TN	1	1,5	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	14.7	14.3	97.6	89.4	97.09	2000	X	X	1	1	2	2	2	5	5	N	N	2	1	100
57	DHAKSHANOMOORTHI	654584D	F	34	TN	1	1	1	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	15.8	15	94.3	86.2	184.1	1011	15	X	1	1	2	2	2	2	2	N	N	1	1	100
59	MAHENDRA SINGH BISHT	747960D	M	51	CHAT	1	9	1	2	1	2	2	2	1	1	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	15.3	14.5	X	X	50.45	1377	X	X	1	1	2	2	2	3	3	N	MILD CHRONIC ILEITIS	2	1	100
60	GOPAL RAO R	762321D	M	24	CHAT	1	1	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	15.4	16.3	79.6	79.9	125.8	956.3	41	X	1	2	1	2	2	2	5	N	N	1	1	90
2	SARAVANAN M	471116D	M	29	TN	2	2	1	2	2	2	2	2	2	1	2	2	2	2	2	2	2	1	1	2	2	2	2	2	2	14.9	X	101	X	92.78	X	31.6	X	2	2	2	1	1	2	1	MILD CHRONIC DUODENITIS	MILD VILLOUS ATROPHY	1	X	X
4	RAVI PRASAD TIWARI	562944D	M	25	JHA	2	1	1	2	2	2	2	1	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	16	14.6	96.4	93.4	165.4	168.8	16.5	X	2	1	2	2	2	2	2	N	MILDEOSNOPHILICILEITIS	1	1	80
5	SARASWATHY	803373B	F	23	TN	2	0	1	2	2	2	2	1	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	12	11.3	95.6	95.5	199.2	421.9	32	12	1	2	2	1	1	2	1	N	X	1	1	100
6	LAKSHMI NARAYANAN	588681D	M	58	TN	2	5	1	2	2	2	2	2	2	1	1	2	2	2	2	2	2	2	2	1	2	2	2	2	2	13.9	X	87.2	X	191.7	X	28.2	X	2	2	2	1	2	2	2	N	N	1	X	X
7	VICTORIA	344627	F	39	TN	2	1,6C	2	2	2	2	2	2	2	2	1	1	2	2	2	2	1	2	2	2	2	2	2	2	2	8.6	11.5	81.5	92.2	112.5	739.4	25	X	1	1	2	2	2	2	2	N	N	1	1	100
11	MUNASWAMY NAIDU	587924D	M	56	AP	2	3	1	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	13.4	12.2	98.5	94.5	149.9	623.7	30.2	21.5	1	1	2	1	2	3	1	MILD CHRONIC DUODENITIS	N	2	1	100
13	MANTU SHARMA	601655D	M	22	JHA	2	7A	1	2	2	2	2	2	1	1	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	13.9	X	88.6	X	180.3	X	16.5	X	2	2	2	2	2	2	2	N	CHRONIC ACTIVE ILEITIS	1	X	X
14	JAMBU LINGAM A K	364766B	M	66	TN	2	3	1	2	2	2	2	2	2	1	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	11.6	15.7	94.9	94.2	130	175.8	53.7	X	2	2	2	2	2	2	1	MILD CDUODENITIS, VILLOUS ATR	N	1	1	100
19	SHOBHA JAIN	610165D	F	46	BIHAR	2	5	1	2	2	2	2	1	1	2	2	1	2	2	2	2	2	2	2	1	2	2	2	2	2	11	11.2	86.3	84.4	195.8	662	26.5	7.34	1	X	X	2	1	5	5	N	N	2	3	100
21	KRISHNAVENI SIRIBOYINA	631316D	F	33	AP	2	7A	1	2	2	2	2	1	1	1	1	1	1	1	1	2	2	2	2	2	2	1	2	2	2	9.8	10.1	94.2	93	83	293	57.1	X	1	2	2	2	2	2	3	N	N	1	1	100
22	NAROTTAM SAHOO	842497B	M	41	ORISSA	2	1	1	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	8.7	9.8	74.6	74	163.9	339.5	32.4	X	1	1	2	2	2	2	3	N	PROMINENT LYMPHOID F	1	1	90
24	PINTU KHETAN	654648D	M	28	ASSAM	2	2,7A	1	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	1	2	1	2	2	2	8.9	X	129	X	125.2	X	61	X	2	2	2	2	1	2	2	MODERATE VILLOUS ATROPHY	INCREASED IEL	1	X	X
27	BAGAVATHI	736460A	F	65	AP	2	7A	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	1	2	2	2	8.3	13	70.3	90.6	179.6	229.4	22	X	1	2	2	2	2	2	2	N	X	1	1	100
28	SAUNDAR RANI G	067144D	F	48	TN	2	7A	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	9.2	9	X	69.1	194.4	314.1	9.5	6.3	1	2	2	2	2	2	2	N	N	1	3	90
30	MEERA SINGH	656261D	F	35	JHA	2	2	1	2	2	2	2	1	1	1	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	8.1	13	133	82.4	163.1	507	41.8	X	1	2	2	2	1	3	1	MILD CDUODENITIS, HIGH IEL	X	2	1	100
31	ISWARA MAHARANA	078890D	M	52	ORISSA	2	1	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	10.5	X	102	X	123.6	X	56	X	2	1	2	2	2	2	2	N	N	1	X	X
32	PULIN CHANDRA SADHU	656194D	M	63	WB	2	3	1	2	2	2	2	2	1	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	10	11.5	89	89.5	148.9	652.4	24.6	7.8	1	2	2	2	2	3	1	N	N	2	1	100
37	VINAYAGAM P	623789D	M	29	TN	2	3	1	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	14.4	15.7	93.7	95.7	175.2	581.3	26.5	X	1	2	2	2	2	1	1	N	MILD ACUTE ILEITIS	2	1	100
38	ANIL KUMAR MANDAL	540702D	M	45	JHA	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	11.2	13.2	110	91.9	94.46	498.8	X	11.8	1	1	2	2	1	5	3	N	X	2	1	90
39	PREETHAM SAMUEL	7293000	M	32	TN	2	1	1	2	2	2	1	1	1	1	2	2	2	2	2	2	2	1	1	2	2	2	2	2	2	11.8	X	90.8	X	135.3	X	X	X	2	1	1	2	2	4	4	N	X	2	X	X
40	MANJUNATHAN D	750023B	M	28	TN	2	1,5	1	2	2	2	1	1	2	1	2	2	2	2	2	2	2	2	2	1	2	1	2	2	2	9.7	12.4	X	73.4	48.58	387.5	134	X	1	1	2	2	2	5	3	N	N	2	1	100
43	KANAKARAO	714518D	M	23	AP	2	0	1	2	1	2	1	1	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	16.8	16.9	89.9	82.9	136.7	675.4	42.8	30.5	1	2	2	2	2	1	1	N	N	2	1	100
45	BHABANI UPADHAYAYA	737864D	F	51	TN	2	1,3	1	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	13.1	13.8	91.9	93.6	153.8	593.4	X	23.6	1	1	2	2	2	2	3	INCREASED IEL,VILLOUS ATROPH	N	1	1	90
47	SARANYA	010013B	F	18	TN	2	0	1	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	10	12.7	66.9	79.6	134.3	623	38	X	1	2	2	2	2	1	1	N	X	2	1	100
49	SELVARANI A	798784C	F	24	TN	2	0	2	2	2	2	2	2	1	1	2	2	2	2	2	1	2	2	2	2	2	1	2	2	2	9.9	11.1	87	85	175.8	476.2	23.3	X	1	2	2	X	2	2	1	N	ACUTE ILEITIS	1	1	100
50	ANIL KUMAR MAHATO	782527D	M	21	WB	2	7A	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	13.8	14	98.9	94.5	145	543.4	X	X	1	2	2	1	2	2	2	N	N	1	3	100
54	ANIL KUMAR	774756D	M	35	BIHAR	2	5	1	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	12.8	X	88.8	X	187.5	X	X	X	2	2	2	1	2	1	1	INCREASED IEL	N	2	X	X
55	APURBA KUMAR SHARMA	723845D	M	37	WB	2	7A	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	14.3	14.2	93.9	92.4	199	683.3	X	11.8	1	2	2	2	2	2	5	X	X	1	1	100
56	DEEPAK S	526554A	M	25	TN	2	1	1	2	2	2	2	1	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	12.9	14.1	80.8	79.7	168.7	556.3	26	12.4	1	1	1	2	2	1	1	N	N	2	1	100
58	SAKUNTHALA K	190768D	F	62	TN	2	9	1	2	2	2	2	2	1	2	1	1	2	2	2	2	2	2	2	2	1	2	2	2	2	11.3	X	83.8	X	141	X	X	X	2	2	2	2	2	3	3	N	N	2	X	X
X1	DEVAKI	124100C	F	51	TN	3	1,6A	1	2	2	2	2	1	2	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	12	X	83.4	X	112.7	X	21.2	X	X	1	1	2	1	2	3	N	X	1	X	X
X2	AKILESH KUMAR SINGH	578322D	M	46	JHA	3	7B	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	12.3	X	93.8	X	167.8	X	12.5	X	X	2	2	2	2	3	3	MILD DUODENITIS	N	2	X	X
X3	SUBRAMANI C	261369C	M	58	TN	3	1	1	2	2	2	2	1	2	1	1	2	2	2	2	2	2	2	2	2	2	1	2	2	2	16.2	X	93.6	X	126.9	X	16.5	X	X	1	2	2	2	5	5	N	X	2	X	X
X4	PYNHUNLANG LYNGDOH	614845D	M	18	MEGHA	3	7B	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	15	X	88.3	X	173.3	X	19	X	X	2	2	2	2	3	3	N	N	2	X	X
X5	TOTAN CHAKRABORTHY	647471D	M	34	TRIPU	3	7A	1	2	2	2	2	2	1	1	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	13.1	X	69	X	161.4	X	17.8	X	X	2	2	2	2	2	2	N	N	1	X	X
X6	LAKHAN LAL BARNWAL	587064D	M	50	JHA	3	1,5	1	2	1	2	2	2	2	1	2	1	2	2	2	1	2	2	2	1	2	2	2	2	2	12.2	X	83.5	X	143.3	X	19.1	X	X	1	2	2	2	2	5	N	N	1	X	X
X7	DEBURANJAN MOZUMDER	152795C	M	47	WB	3	7A	1	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	14.2	X	X	X	133	X	43.6	X	X	2	2	2	2	2	2	N	CHRONIC ACTIVE ILEITIS	1	X	X
X8	SHASHI KALA DEVI	710386D	F	46	JHA	3	1	1	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	12.3	X	87.2	X	125.2	X	18.2	X	X	2	1	2	2	2	2	N	MINIMAL ACUTE ILEITIS	1	X	X
X9	SRINIVASAN B	684799C	M	46	TN	3	1,5	1	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	15.1	X	108	X	86.22	X	X	X	X	1	2	2	1	2	2	MILD CHRONIC DUODENITIS	X	1	X	X
X10	KARPAGAM	782465D	F	49	TN	3	8,4B	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	8.1	X	63.4	X	144.2	X	X	X	X	2	2	2	X	2	3	N	CHRONIC ACTIVE ILEITIS	1	X	X
X11	MANOJ PANDEY	519746D	M	29	JHA	3	1	1	2	1	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	15.4	X	80.4	X	189	X	X	X	X	1	1	2	2	2	2	N	PROMINENT LYMPHOID F	1	X	X
X12	MALAY KUMAR	557236D	M	47	WB	3	1	1	2	2	2	1	1	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	8.3	X	122	X	62.48	X	X	X	X	1	1	2	2	3	3	N	N	2	X	X

R N	NAME	HOS NO	G	A	STATE	CAT	DX	S	S1	S2	S3	S4	S5	S6	S7	DM	HT	IHD	DL	CV	D1	D2	SM	AL	DE	SX	F1	F2	F3	F4	HB1	HB2	MC1	MC2	B12A	B12B	HC1	HC2	RX	AP	IF	SP	TTG	HPA	HPF	HPD	HPI	HP	SUB	COM
1	KRISHNA PRASAD RAJA	575993	D	M	44	KERALA	1	1,5	1	2	2	2	2	1	2	1	2	2	2	2	2	2	1	2	1	2	2	2	2	13.1	13.3	88	86.2	157.2	1005	13.2	X	1	2	1	2	1	3	3	N	X	2	1	100
3	BASANTH MAHTO	589418	D	M	47	JHA	1	7A	1	2	2	2	2	1	2	1	2	2	2	2	2	2	2	2	2	2	1	2	2	6.1	6.9	81.6	90.9	197.7	1495	X	5.9	1	2	2	1	2	2	2	MILD CHRONIC DUODENITIS	X	1	1	100
8	SANKAR KUMAR GHOSH	316650	D	M	57	WB	1	7A	1	2	2	2	2	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	12.3	14.1	93.1	94.7	189	1284	X	21	1	1	2	2	2	2	2	N	N	1	1	100
9	SULEKHA DEY	610095	D	F	44	ASSAM	1	7A	1	2	2	2	2	1	1	1	2	2	2	2	2	2	2	2	2	2	1	2	2	9.8	8.4	59.7	59	124.9	381.4	31.9	X	1	2	2	2	1	2	2	N	X	1	3	80
10	SEKAR J	576351	D	M	42	AP	1	5,7A	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	15.5	15	94.5	93.2	131.3	772.3	22.5	15.4	1	2	2	2	2	2	2	N	N	1	3	100
12	RAGHUNATH REDDY	609122	D	M	43	AP	1	2,7A	1	2	1	2	1	1	1	2	2	2	2	2	2	2	1	1	2	2	1	2	2	1	6.6	15.4	129	X	78.01	680.5	94.6	X	1	2	2	2	1	2	2	MILD VILLOUS ATROPHY	N	1	1	100
15	ANUGRAH N SINGH	618868	D	M	51	JHA	1	2	1	2	2	2	2	1	1	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	9.9	13.5	110	87.8	88.04	293.4	42.5	X	1	2	2	2	2	3	3	SUBTOTAL VILLOUS ATROPHY	N	2	1	100
16	ANTAKA TAMANG	617252	D	F	38	WB	1	1,6A	1	2	2	2	2	2	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	12.1	12.2	89.3	85.7	194.1	843.3	22		1	1	2	2	2	2	2	MILD CHRONIC DUODENITIS	N	1	1	100
17	SURESH KUMAR PATEL	437690	D	M	43	MP	1	7A	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	1	2	2	2	2	2	13.1	X	94.4	X	187.9	X	15.2	X	2	2	2	2	2	2	2	N	N	1	X	X
18	MENUKA DANGAL	627493	D	F	43	NEPAL	1	0	1	2	1	2	2	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	13.1	13.1	98.8	94.2	197.4	1858	14	9.81	1	2	2	1	2	1	1	N	X	2	1	100
20	KATHIRVEL S	598782	D	M	57	TN	1	5,6C	2	2	2	2	2	2	2	1	1	2	2	2	2	1	2	2	1	2	2	1	2	2	14.5	12.2	87.9	85.7	138	843.3	32.7	X	1	2	2	2	2	2	2	N	N	1	3	100
23	SUSANTHA MONDAL	647840	B	M	42	WB	1	1	1	2	2	2	2	1	2	1	2	1	2	2	2	2	2	2	2	2	2	2	2	13.2	14	85.8	88.2	196	948.7	X	X	1	1	2	2	2	2	2	MILD CHRONIC DUODENITIS	MILD ACTIVE ILEITIS	1	3	100
25	PRABIR KUMAR ROY	653180	D	M	44	WB	1	1	1	2	2	2	2	1	1	2	2	2	2	2	2	2	1	2	2	2	2	2	2	11.1	12.5	82.9	75.2	160.7	1577	59.7	X	1	2	1	2	2	2	5	N	N	1	1	100
26	SYED SHAID R	665073	D	M	36	TN	1	3	1	2	2	2	2	1	1	2	2	2	2	2	2	2	1	1	2	2	2	2	2	14.9	18.3	118	100	97.55	209.6	X	X	1	1	2	2	2	2	1	INCREASED IEL,VILLOUS ATROPH	X	1	1	100
29	PRASAD AL	623593	D	M	41	JHA	1	6B,7A	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	13.8	12.9	86.4	86.4	136.6	888.1	29.2	X	1	2	2	2	1	2	2	MILD CHRONIC DUODENITIS	N	1	1	100
33	ARUN KUMAR TANTI	391770	D	M	42	JHA	1	0	1	2	2	2	2	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	12.4	14.1	91.4	78	96.2	860.4	39.9	X	1	2	2	2	1	1	1	N	N	2	1	100
34	ANJU DEVI	654619	D	M	40	JHA	1	0	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	10.3	12.4	75	85	126.5	1029	16.2	X	1	2	2	2	1	1	1	N	N	2	1	100
35	RADHE SHYAM MANDAL	186959	D	M	53	NEPAL	1	5	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	1	2	2	2	2	2	13.3	13.5	95.8	92.3	136.8	1420	25.5	X	1	2	2	2	2	2	1	N	N	1	1	90
36	CHINNA THAMBI	701111	A	M	47	TN	1	1	1	2	2	2	2	1	2	2	2	2	2	2	2	2	1	2	2	2	1	2	2	8.9	13.1	62	X	140.2	1460	X	X	1	1	1	2	2	4	4	LYMPHANGEIECTASIS	N	2	1	100
41	PARIMALA	641784	D	F	40	AP	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	8.4	13.1	70.8	85.7	86	340.5	X	9	1	1	1	2	2	4	1	X	X	2	3	100
42	BIPUL ROY	709948	D	M	30	WB	1	0	1	2	2	2	2	2	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	14.1	14.9	88	87.6	189.8	930.6	49	X	1	2	2	2	2	2	1	N	N	1	1	100
44	DEBABRATA DEY	914627	C	M	61	WB	1	2	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	11.2	11.7	119	93.6	179.5	2000	X	X	1	2	2	2	1	1	5	INCREASED IEL,VILLOUSATROPH	MILD CHRONIC ILEITIS	2	1	100
46	DHAMAYANTHI	702010	D	M	39	TN	1	1	1	2	2	2	1	1	1	1	2	2	2	2	2	2	2	2	2	2	1	2	2	9	X	64.6	X	172.5	X	X	X	2	1	2	1	2	2	2	N	X	1	X	X
48	SAMPATH S	562950	D	M	54	TN	1	6A,7A	1	2	1	2	2	1	2	1	2	2	2	2	2	1	2	2	2	2	2	2	2	14.6	X	89.5	X	170.3	X	X	X	2	2	2	2	2	2	2	MILD CHRONIC DUODENITIS	N	1	X	X
51	JAGADISH PRASAD SAH	717824	D	M	65	JHA	1	7A	1	2	2	2	2	1	1	2	1	2	2	2	2	2	2	2	2	2	2	2	2	14	14.2	71.3	73	184.9	2000	22.5	X	1	2	2	2	2	2	2	N	N	1	1	100
52	BIKAS KUMAR SAHU	723577	D	M	29	JHA	1	7A	1	2	2	2	2	2	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	14.5	14.1	92.6	88.3	166.5	2000	17.4	11.3	1	2	2	2	2	2	2	N	N	1	1	100
53	JOTHI LINGAM	293387	D	M	50	TN	1	1,5	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	14.7	14.3	97.6	89.4	97.09	2000	X	X	1	1	2	2	2	5	5	N	N	2	1	100
57	DHAKSHANOMOORTHI	654584	D	F	34	TN	1	1	1	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	15.8	15	94.3	86.2	184.1	1011	15	X	1	1	2	2	2	2	2	N	N	1	1	100
59	MAHENDRA SINGH BISHT	747960	D	M	51	CHAT	1	9	1	2	1	2	2	2	1	1	2	2	2	2	2	2	2	2	1	2	2	2	2	15.3	14.5	X	X	50.45	1377	X	X	1	1	2	2	2	3	3	N	MILD CHRONIC ILEITIS	2	1	100
60	GOPAL RAO R	762321	D	M	24	CHAT	1	1	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	15.4	16.3	79.6	79.9	125.8	956.3	41	X	1	2	1	2	2	5	N	N	1	1	90
2	SARAVANAN M	471116	D	M	29	TN	2	2	1	2	2	2	2	2	1	2	2	2	2	2	2	2	1	1	2	2	2	2	2	14.9	X	101	X	92.78	X	31.6	X	2	2	2	2	1	1	2	MILD CHRONIC DUODENITIS	MILD VILLOUS ATROPHY	1	X	X
4	RAVI PRASAD TIWARI	562944	D	M	25	JHA	2	1	1	2	2	2	2	1	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	16	14.6	96.4	93.4	165.4	168.8	16.5	X	2	1	2	2	2	2	2	N	MILDEOSNOPHILICILEITIS	1	1	80
5	SARASWATHY	803373	B	F	23	TN	2	0	1	2	2	2	2	1	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	12	11.3	95.6	95.5	199.2	421.9	32	12	1	2	2	2	1	1	2	N	X	1	1	100
6	LAKSHMI NARAYANAN	588681	D	M	58	TN	2	5	1	2	2	2	2	2	1	1	2	2	2	2	2	2	2	2	1	2	2	2	2	13.9	X	87.2	X	191.7	X	28.2	X	2	2	2	1	2	2	2	N	N	1	X	X
7	VICTORIA	344627	F	F	39	TN	2	1,6C	2	2	2	2	2	2	2	1	1	2	2	2	1	2	2	2	2	2	2	2	2	8.6	11.5	81.5	92.2	112.5	739.4	25	X	1	1	2	2	2	2	2	N	N	1	1	100
11	MUNASWAMY NAIDU	587924	D	M	56	AP	2	3	1	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	13.4	12.2	98.5	94.5	149.9	623.7	30.2	21.5	1	1	2	1	2	3	1	MILD CHRONIC DUODENITIS	N	2	1	100
13	MANTU SHARMA	601655	D	M	22	JHA	2	7A	1	2	2	2	2	2	1	1	2	2	2	2	2	2	2	2	1	2	2	2	2	13.9	X	88.6	X	180.3	X	16.5	X	2	2	2	2	2	2	2	N	CHRONIC ACTIVE ILEITIS	1	X	X
14	JAMBU LINGAM A K	364766	B	M	66	TN	2	3	1	2	2	2	2	2	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	11.6	15.7	94.9	94.2	130	175.8	53.7	X	2	2	2	2	2	2	1	MILD CDUODENITIS, VILLOUS ATR	N	1	1	100
19	SHOBHA JAIN	610165	D	F	46	BIHAR	2	5	1	2	2	2	2	1	1	2	2	1	2	2	2	2	2	2	1	2	2	2	2	11	11.2	86.3	84.4	195.8	662	26.5	7.34	1	X	X	2	1	5	5	N	N	2	3	100
21	KRISHNAVENI SIRIBOYINA	631316	D	F	33	AP	2	7A	1	2	2	2	2	1	1	1	1	1	1	2	2	2	2	2	2	2	1	2	2	9.8	10.1	94.2	93	83	293	57.1	X	1	2	2	2	2	3	N	N	1	1	100
22	NAROTTAM SAHOO	842497	B	M	41	ORISSA	2	1	1	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	8.7	9.8	74.6	74	163.9	339.5	32.4	X	1	1	2	2	2	3	N	PROMINENT LYMPHOID F	1	1	90
24	PINTU KHETAN	654648	D	M	28	ASSAM	2	2,7A	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	1	2	1	2	2	8.9	X	129	X	125.2	X	61	X	2	2	2	2	1	2	2	MODERATE VILLOUS ATROPHY	INCREASED IEL	1	X	X
27	BAGAVATHI	736460	A	F	65	AP	2	7A	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	1	2	2	8.3	13	70.3	90.6	179.6	229.4	22	X	1	2	2	2	2	2	2	N	X	1	1	100
28	SAUNDAR RANI G	067144	D	F	48	TN	2	7A	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	9.2	9	X	69.1	194.4	314.1	9.5	6.3	1	2	2	2	2	2	2	N	N	1	3	90
30	MEERA SINGH	656261	D	F	35	JHA	2	2	1	2	2	2	2	1	1	2	2	2	2	2	2	2	2	2	2	2	1	2	2	8.1	13	133	82.4	163.1	507	41.8	X	1	2	2	2	1	3	1	MILD CDUODENITIS, HIGH IEL	X	2	1	100
31	ISWARA MAHARANA	078890	D	M	52	ORISSA	2	1	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	10.5	X	102	X	123.6	X	56	X	2	1	2	2	2	2	2	N	N	1	X	X
32	PULIN CHANDRA SADHU	656194	D	M	63	WB	2	3	1	2	2	2	2	2	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	10	11.5	89	89.5	148.9	652.4	24.6	7.8	1	2	2	2	2	3	1	N	N	2	1	100
37	VINAYAGAM P	623789	D	M	29	TN	2	3	1	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	14.4	15.7	93.7	95.7	175.2	581.3	26.5	X	1	2	2	2	2	1	1	N	MILD ACUTE ILEITIS	2	1	100
38	ANIL KUMAR MANDAL	540702	D	M	45	JHA	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	11.2	13.2	110	91.9	94.46	498.8	X	11.8	1	1	2	2	1	5	3	N	X	2	1	90
39	PREETHAM SAMUEL	7293000	M	M	32	TN	2	1	1	2	2	2	1	1	1	2	2	2	2	2	2	2	1	1	2	2	2	2	2	11.8	X	90.8	X	135.3	X	X	X	2	2	1	2	2	4	4	N	X	2	X	X
40	MANJUNATHAN D	750023	B	M	28	TN	2	1,5	1	2	2	2	1	1	2	1	2	2	2	2	2	2	2	2	1	2	1	2	2	9.7	12.4	X	73.4	48.58	387.5	134	X	1	1	2	2	2	5	3	N	N	2	1	100
43	KANAKARAO	714518	D	M	23	AP	2	0	1	2	1	2	1	1	1	1	2	2	2	2	2	2	2	2	2	2	2	2	1	16.8	16.9	89.9	82.9	136.7	675.4	42.8	30.5	1	2	2	2	2	1	1	N	N	2	1	100
45	BHABANI UPADHAYAYA	737864	D	F	51	TN	2	1,3	1	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	13.1	13.8	91.9	93.6	153.8	593.4	X	23.6	1	1	2	2	2	2	3	INCREASED IEL,VILLOUS ATROPH	N	1	1	90
47	SARANYA	010013	B	F	18	TN	2	0	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	10	12.7	66.9	79.6	134.3	623	38	X	1	2	2	2	2	1	1	N	X	2	1	100
49	SELVARANI A	798784	C	F	24	TN	2	0	2	2	2	2	2	2	1	1	2	2	2	2	1	2	2	2	2	2	1	2	2	9.9	11.1	87	85	175.8	476.2	23.3	X	1	2	2	X	2	2	1	N	ACUTE ILEITIS	1	1	100
50	ANIL KUMAR MAHATO	782527	D	M	21	WB	2	7A	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	13.8	14	98.9	94.5	145	543.4	X	X	1	2	2	1	2	2	2	N	N	1	3	100
54	ANIL KUMAR	774756	D	M	35	BIHAR	2	5	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	1	2	2	2	2	12.8	X	88.8	X	187.5	X	X	X	2	2	2	1	2	1	1	INCREASED IEL	N	2	X	X
55	APURBA KUMAR SHARMA	723845	D	M	37	WB	2	7A	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	14.3	14.2	93.9	92.4	199	683.3	X	11.8	1	2	2	2	2	2	5	X	X	1	1	100
56	DEEPAK S	526554	A	M	25	TN	2	1	1	2	2	2	2	1	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	12.9	14.1	80.8	79.7	168.7	556.3	26	12.4	1	1	1	2	2	1	1	N	N	2	1	100
58	SAKUNTHALA K	190768	D	F	62	TN	2	9	1	2	2	2	2	2	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	11.3	X	83.8	X	141	X	X	X	2	2	2	2	2	3	3	N	N	2	X	X
X1	DEVAKI	124100	C	F	51	TN	3	1,6A	1	2	2	2	2	1	2	1	2	2	2	2	2	1	2	2	2	2	2	2	2	12	X	83.4	X	112.7	X	21.2	X	X	1	1	2	1	2	3	N	X	1	X	X
X2	AKILESH KUMAR SINGH	578322	D	M	46	JHA	3	7B	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	12.3	X	93.8	X	167.8	X	12.5	X	X	2	2	2	2	3	3	MILD DUODENITIS	N	2	X	X
X3	SUBRAMANI C	261369	C	M	58	TN	3	1	1	2	2	2	2	1	2	1	1	2	2	2	2	2	2	2	2	2	1	2	2	16.2	X	93.6	X	126.9	X	16.5	X	X	1	2	2	2	5	5	N	N	2	X	X
X4	PYNHUNLANG LYNGDOH	614845	D	M	18	MEGHA	3	7B	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	15	X	88.3	X	173.3	X	19	X	X	2	2	2	2	3	3	N	N	2	X	X
X5	TOTAN CHAKRABORTHY	647471	D	M	34	TRIPU	3	7A	1	2	2	2	2	2	1	1	2	2	2	2	2	2	1	2	2	2	2	2	2	13.1	X	69	X	161.4	X	17.8	X	X	2	2	2	2	2	2	N	N	1	X	X
X6	LAKHAN LAL BARNWAL	587064	D	M	50	JHA	3	1,5	1	2	1	2	2	2	2	1	2	1	2	2	2	1	2	2	1	2	2	2	2	12.2	X	83.5	X	143.3	X	19.1	X	X	1	2	2	2	2	5	N	N	1	X	X
X7	DEBURANJAN MOZUMDER	152795	C	M	47	WB	3	7A	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	14.2	X	X	X	133	X	43.6	X	X	2	2	2	2	2	2	N	CHRONIC ACTIVE ILEITIS	1	X	X
X8	SHASHI KALA DEVI	710386	D	F	46	JHA	3	1	1	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	12.3	X	87.2	X	125.2	X	18.2	X	X	2	1	2	2	2	2	N	MINIMAL ACUTE ILEITIS	1	X	X
X9	SRINIVASAN B	684799	C	M	46	TN	3	1,5	1	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	15.1	X	108	X	86.22	X	X	X	X	1	2	2	1	2	2	MILD CHRONIC DUODENITIS	X	1	X	X
X10	KARPAGAM	782465	D	F	49	TN	3	8,4B	1	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	1	2	2	8.1	X	63.4	X	144.2	X	X	X	X	2	2	2	2	X	2	3	N	CHRONIC ACTIVE ILEITIS	1	X	X
X11	MANOJ PANDEY	519746	D	M	29	JHA	3	1	1	2	1	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	15.4	X	80.4	X	189	X	X	X	X	X	1	1	2	2	2	N	PROMINENT LYMPHOID F	1	X	X
X12	MALAY KUMAR	557236	D	M	47	WB	3	1	1	2	2	2	1	1	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	8.3	X	122	X	62.48	X	X	X	X	X	1	1	2	2	3	3	N	N	2	X	X